

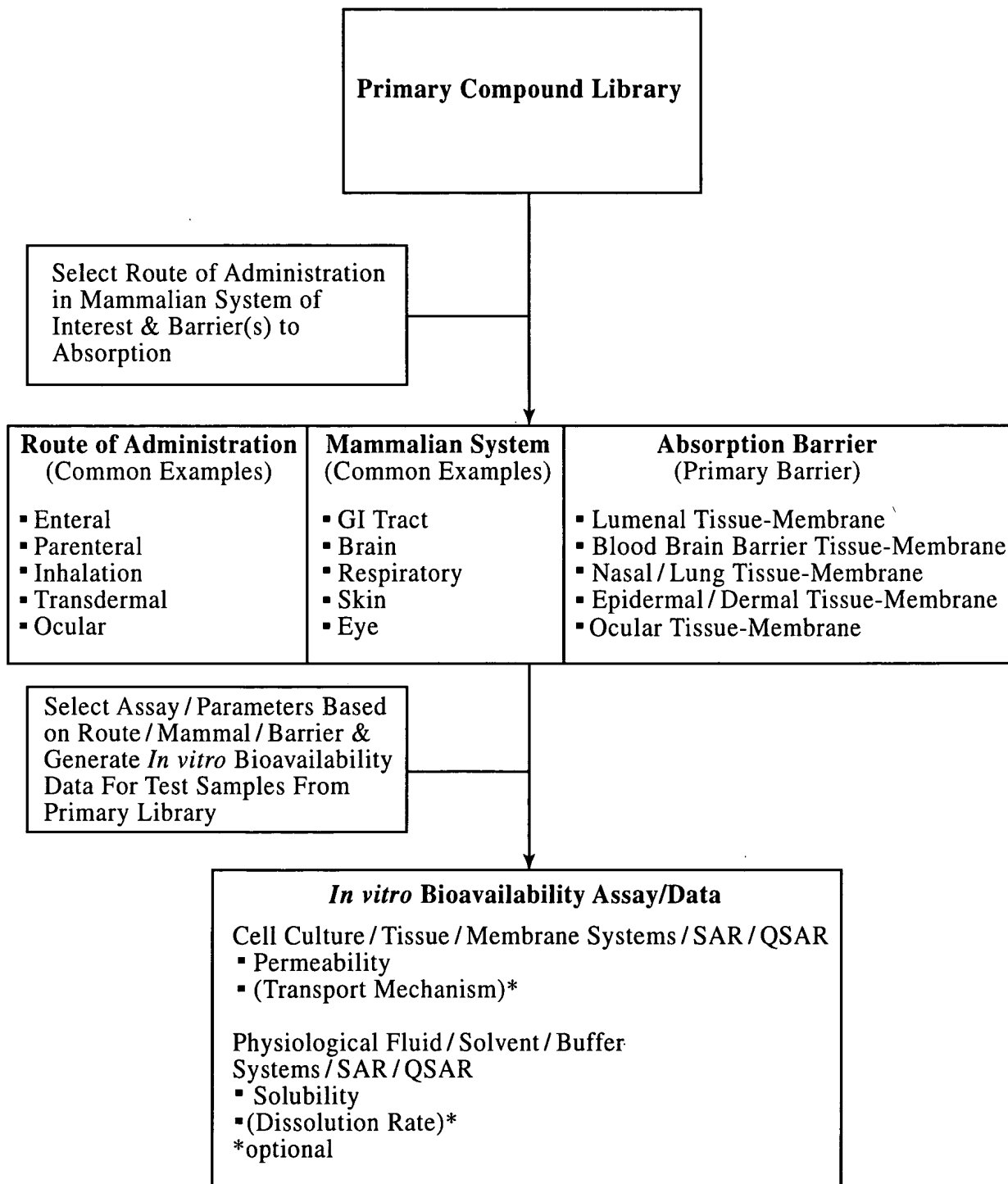
Title: METHOD FOR SCREENING AND
PRODUCING COMPOUND LIBRARIES

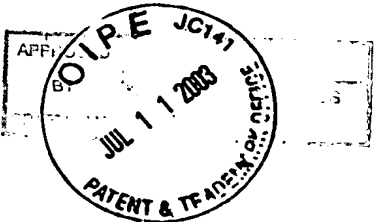
Inventor's Name: GRASS, et al.

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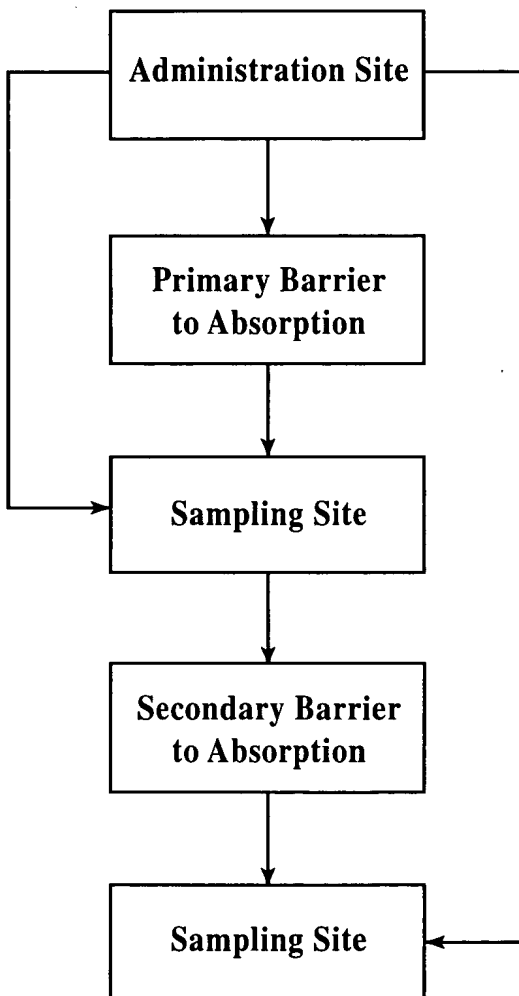
FIG.1

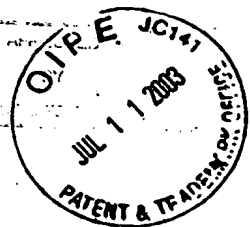




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FIG.2





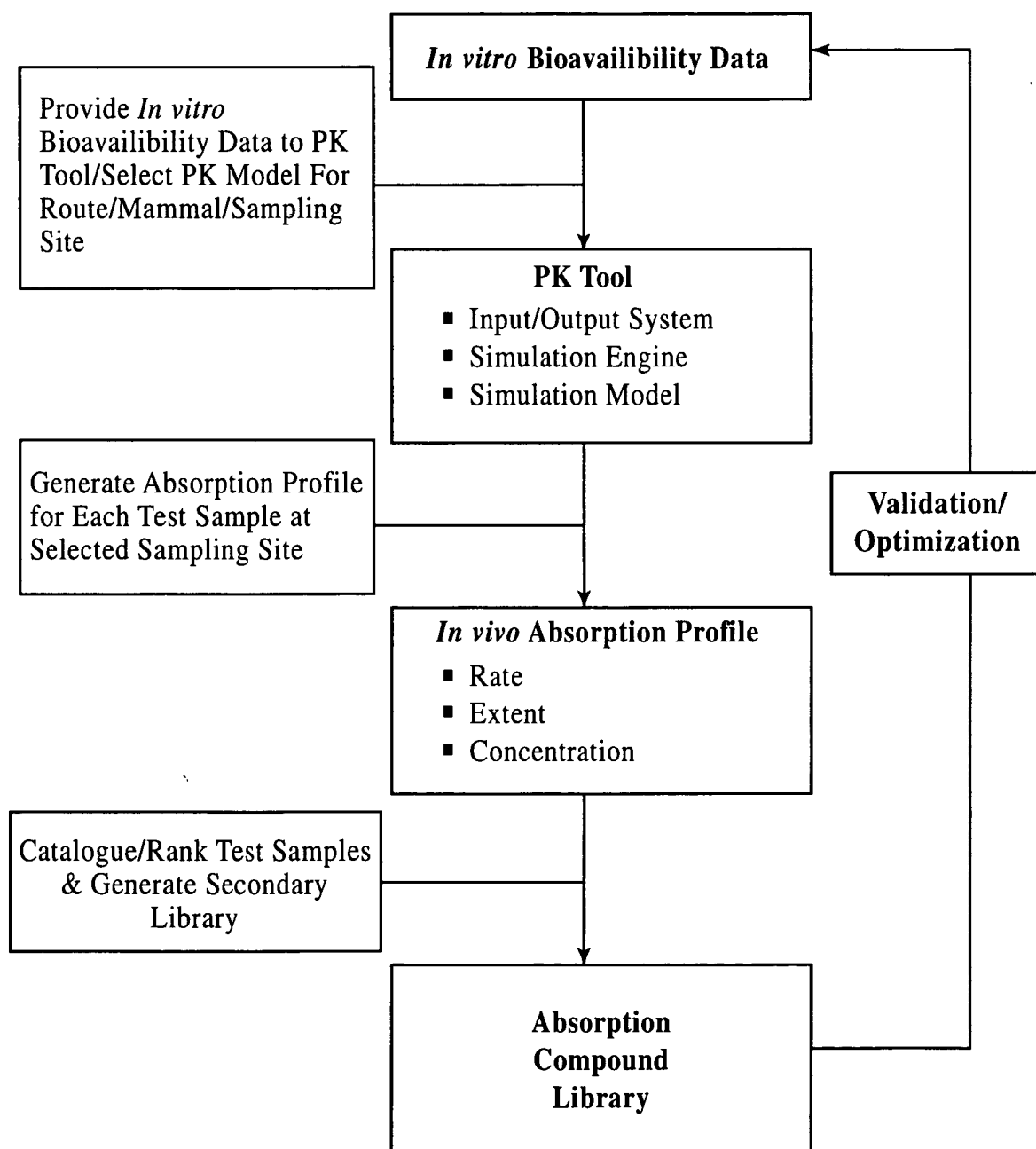
Title: METHOD FOR SCREENING AND
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FIG.3



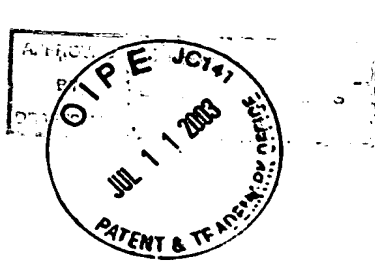


FIG.4

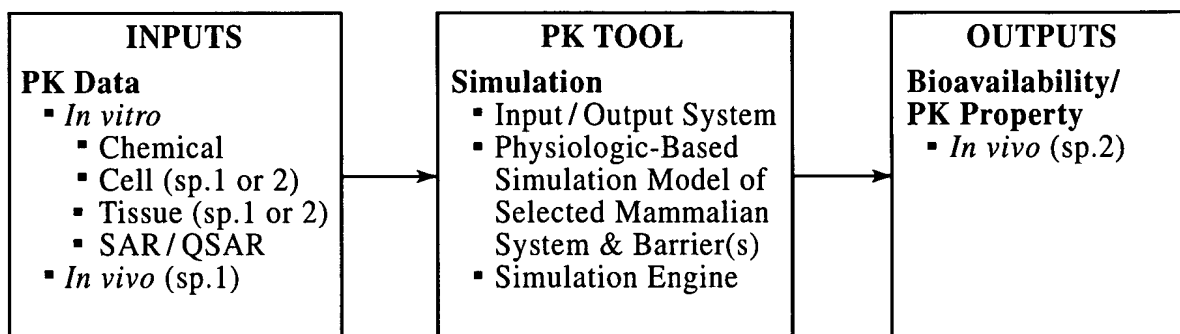
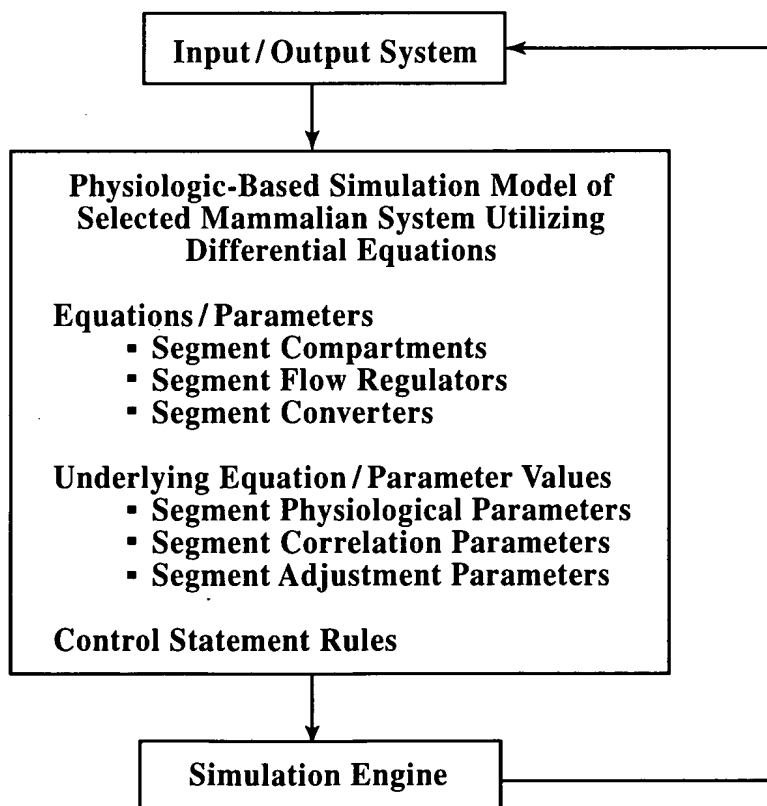
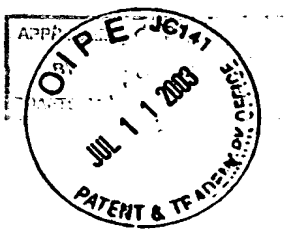


FIG.5





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FIG.6

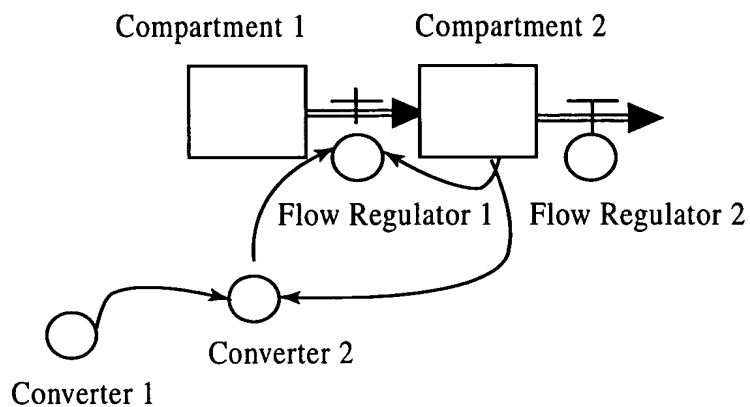

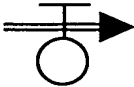


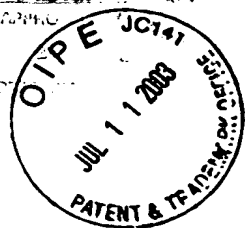


FIG.7

Symbol	Name	Time-Dependent Function
	Compartment	Equation or value for amount of substance stored.
	Flow Regulator	Rate equation for amount of substance transferred.
	Converter	Equation or pre-defined value for (i) input into flow regulator; (ii) input into another converter; and/or (iii) storing value.
	Input Link	Directs input values.



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FIG.8

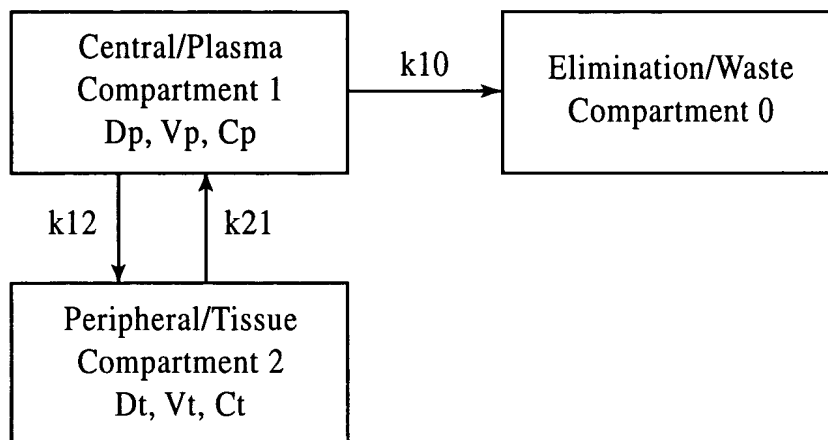
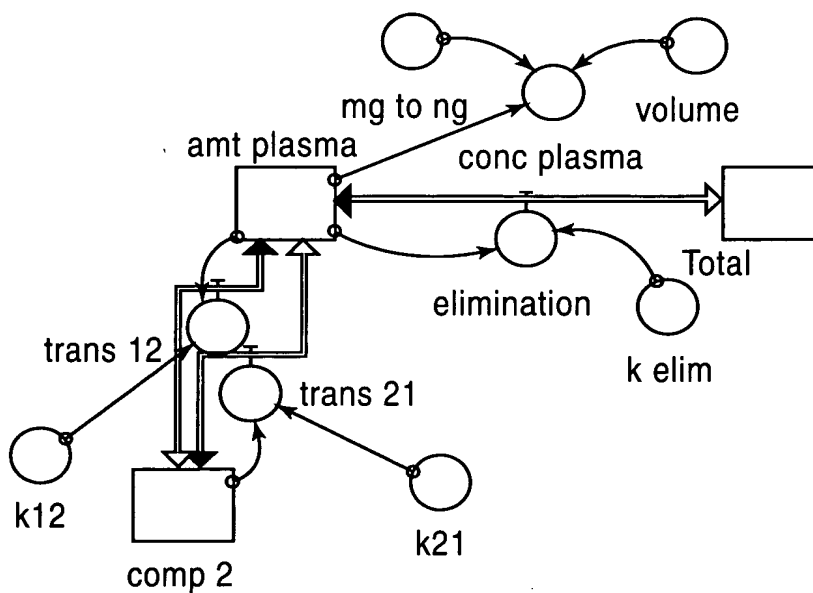


FIG.9



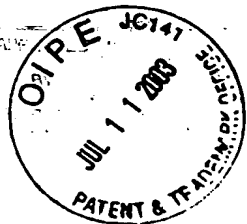
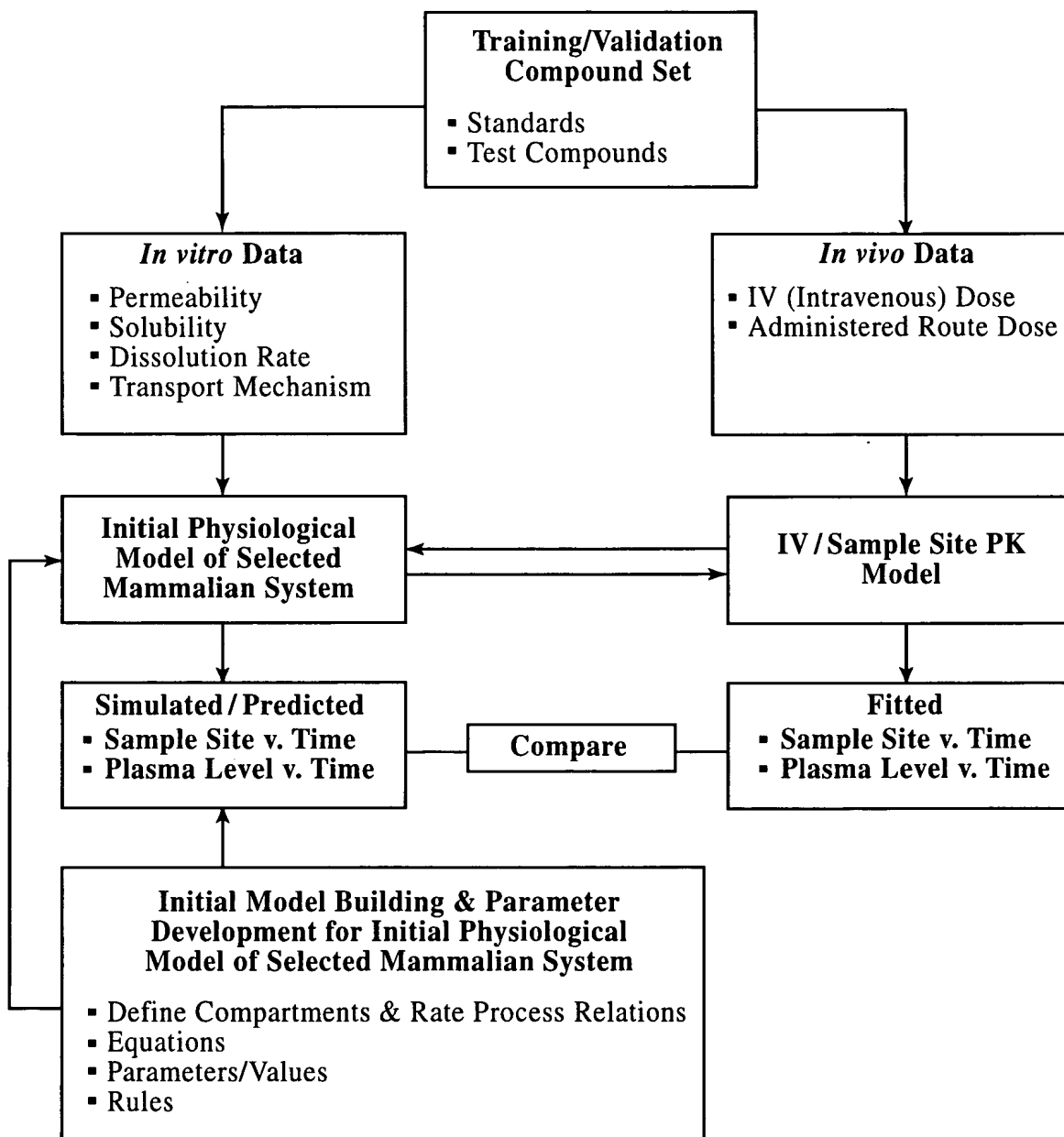


FIG.10



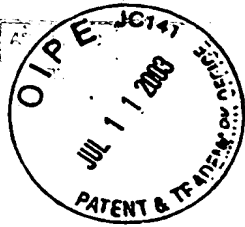
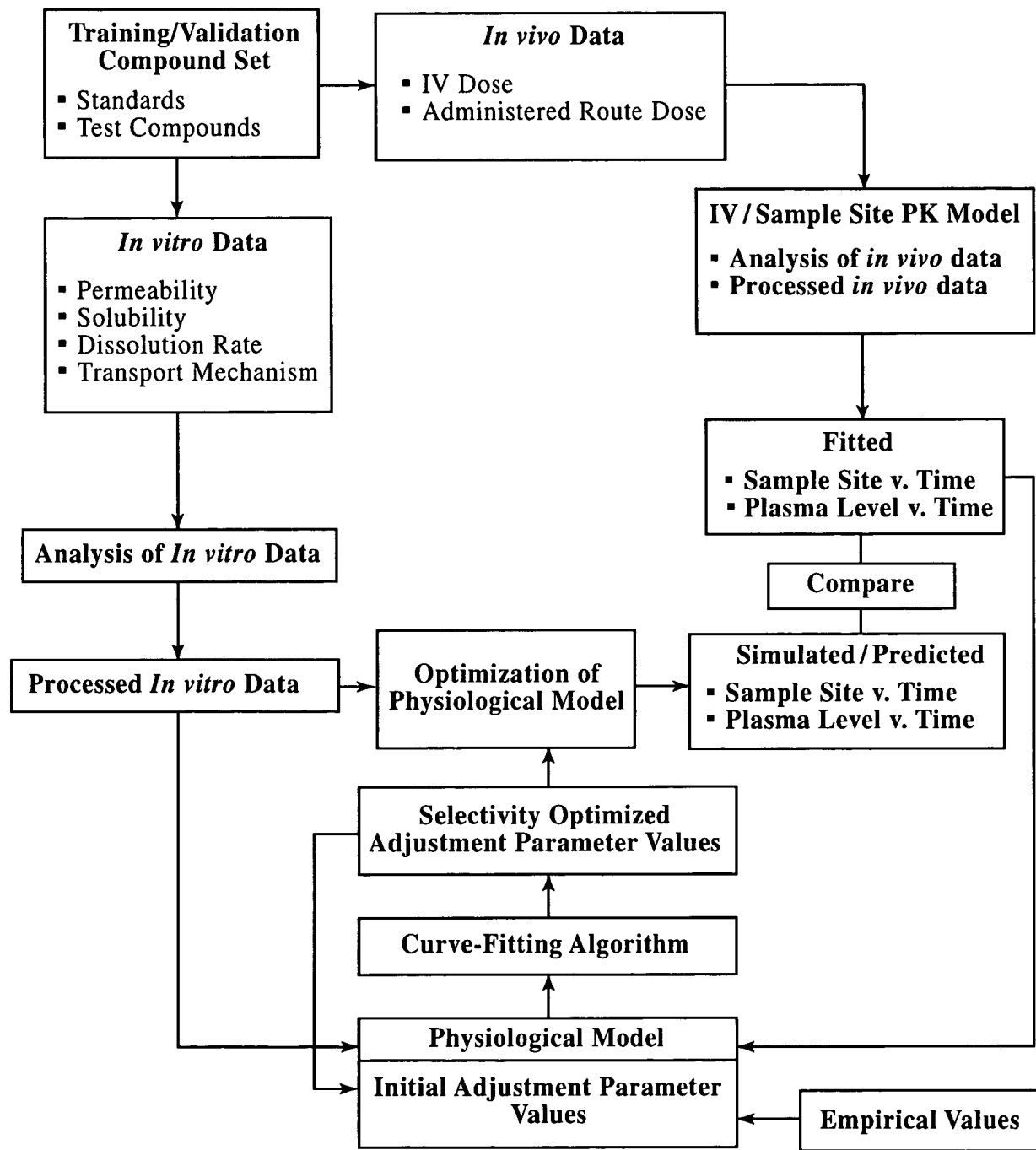


FIG.11



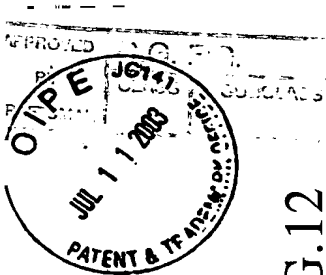
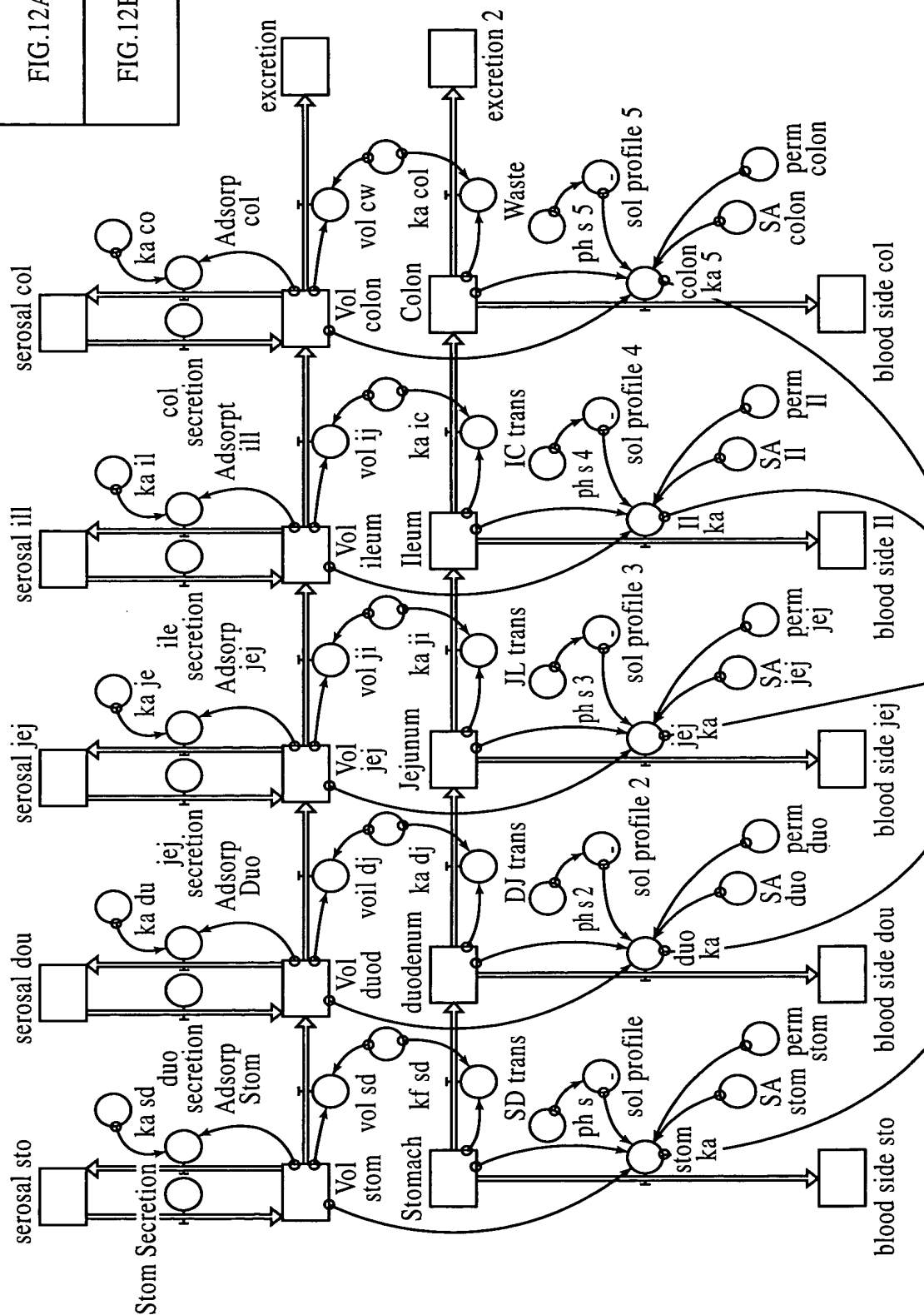
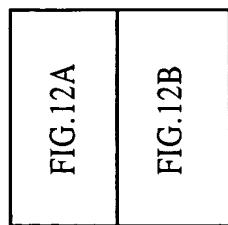


FIG.12A

FIG.12





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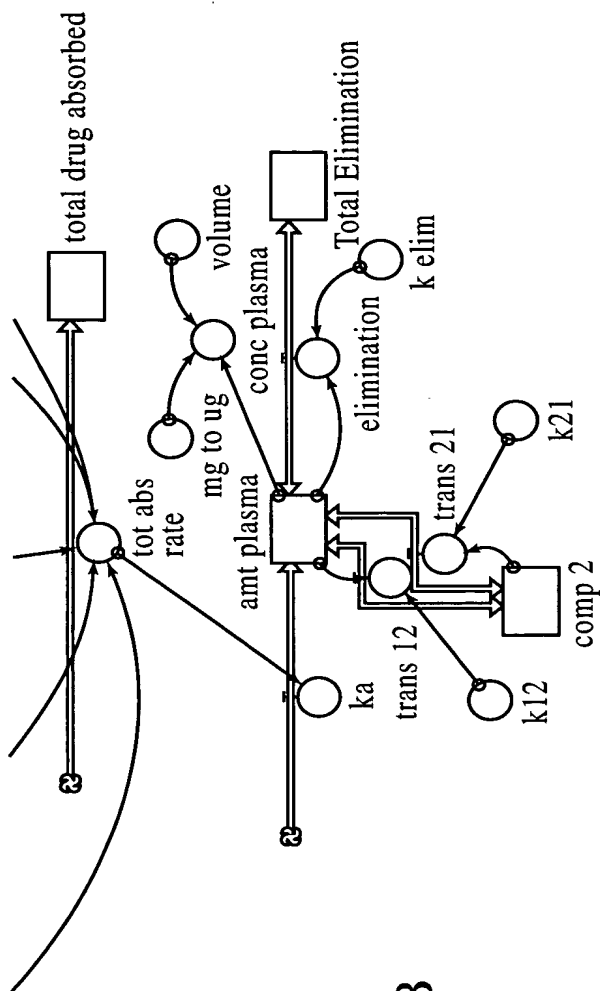
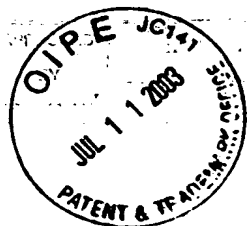


FIG.12B



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FIG.13

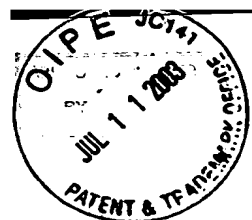
Mass-Volume GI Tract Model

- **GI Segment Compartments**
 - Fluid Volume
 - Fluid Absorption
 - Insoluble Mass
 - Soluble Mass Absorption
- **GI Segment Flow Regulators**
 - Fluid Volume Absorption Rate
 - Fluid Volume Secretion Rate
 - Fluid Volume GI Transit Rate
 - Insoluble Mass GI Transit Rate
 - Soluble Mass Absorption Rate
- **GI Segment Converters**
 - Rate Constant
 - pH
 - Solubility
 - Surface Area
 - Permeability

FIG.14

Mass-Volume GI Tract Model

- **GI Segment Compartments & Flow Regulators**
 - **Fluid Volume**
 - *Fluid Volume Absorption Rate*
 - *Fluid Volume Secretion Rate*
 - *Fluid Volume GI Transit Rate*
 - **Fluid Volume Absorption**
 - *Fluid Volume Absorption Rate*
 - *Fluid Volume Secretion Rate*
 - **Insoluble Mass**
 - *Insoluble Mass GI Transit Rate*
 - *Soluble Mass Absorption Rate*
 - **Soluble Mass Absorption**
 - *Soluble Mass Absorption Rate*



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FIG.15

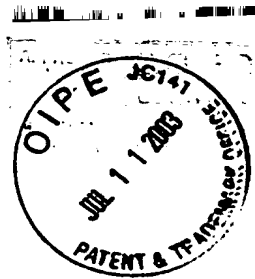
Mass-Volume GI Tract Model

- **GI Segment Flow Regulators & Converters**
 - **Fluid Volume Absorption Rate**
 - *Fluid Volume Absorption Rate Constant*
 - **Fluid Volume Secretion Rate**
 - *Fluid Volume Secretion Rate Constant*
 - **Fluid Volume GI Transit Rate**
 - *Fluid Volume GI Transit Rate Constant*
 - **Insoluble Mass GI Transit Rate**
 - *Insoluble Mass GI Transit Rate Constant*
- **Soluble Mass Absorption Rate**
 - *Fluid Volume*
 - *Insoluble Mass*
 - *Mass Solubility Profile*
 - *pH*
 - *Permeability*
 - *Surface Area*

FIG.16

Mass-Volume GI Tract Model

- **GI Segment Converters**
 - Rate Constant
 - pH
 - Solubility
 - Surface Area
 - Permeability



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FIG.17

ICM 1505 v. Mass GI Tract Model

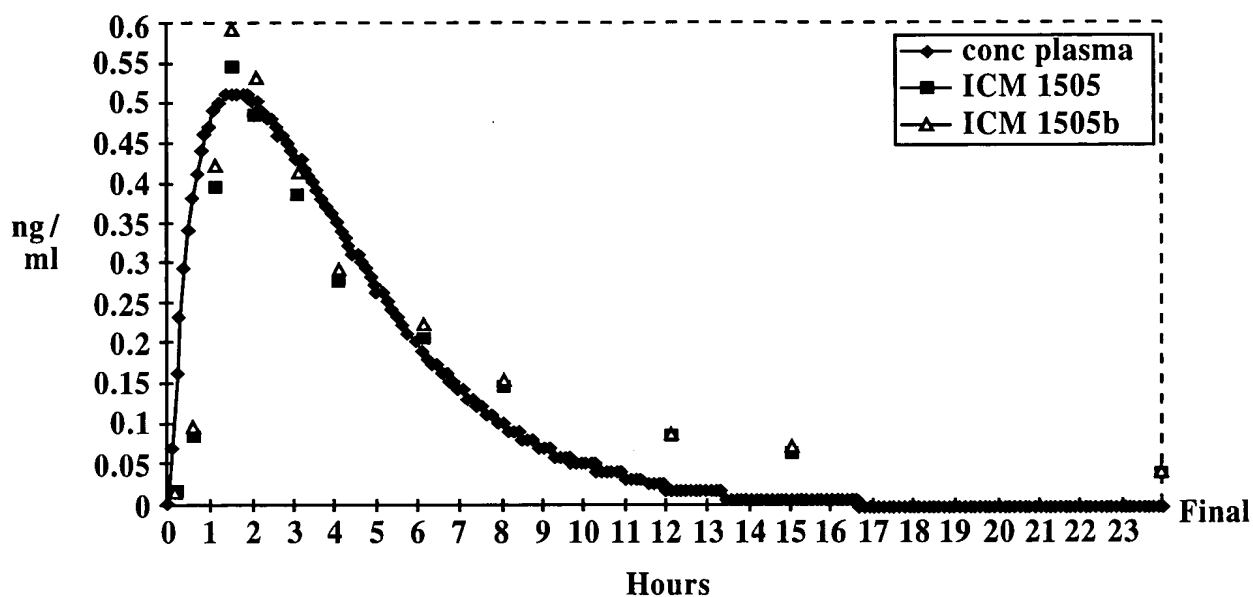
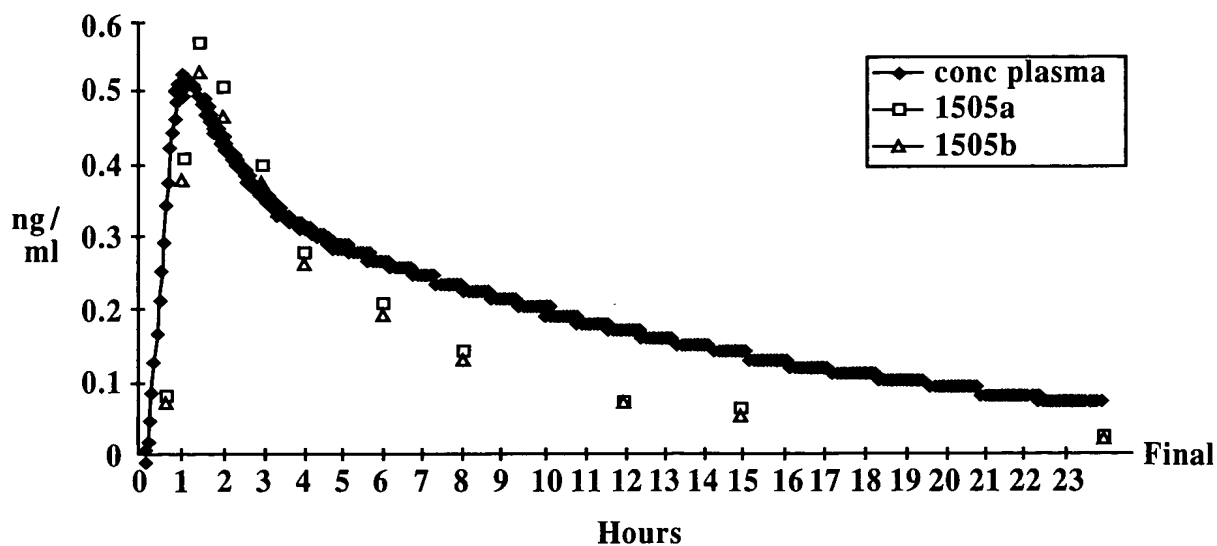
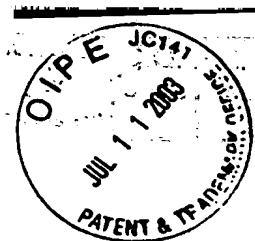


FIG.18

ICM 1505 v. Mass-Volume GI Tract Model





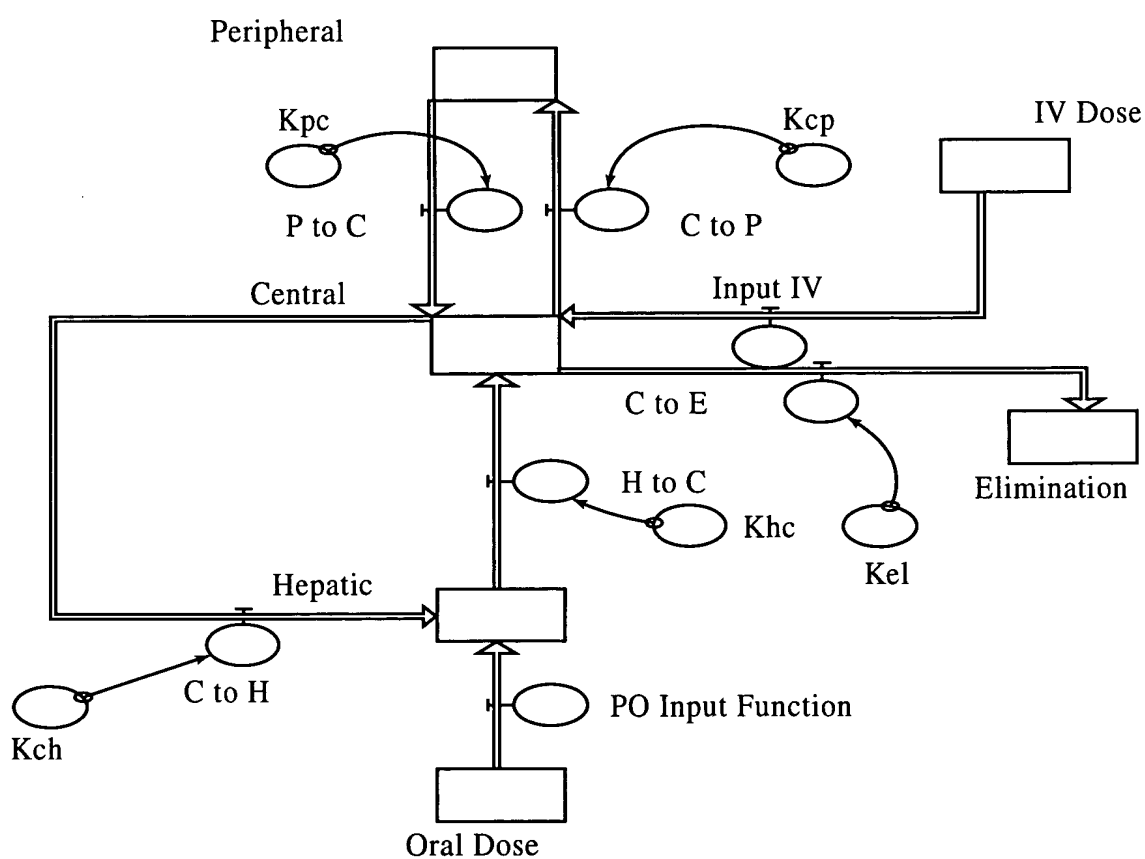
Title: METHOD FOR SCREENING AND
PRODUCING COMPOUND LIBRARIES

Inventor's Name: GRASS, et al.

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FIG.19



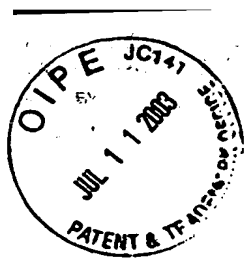
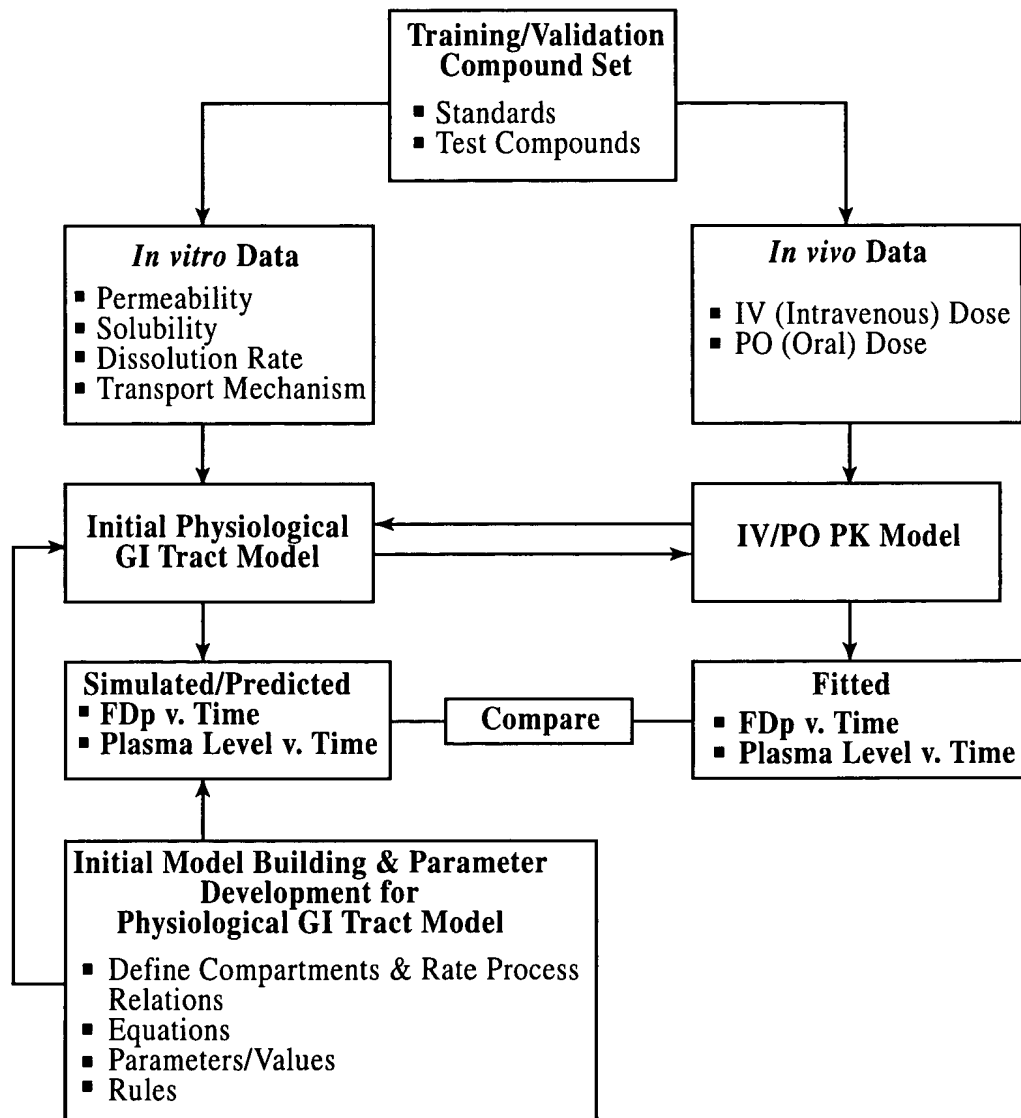
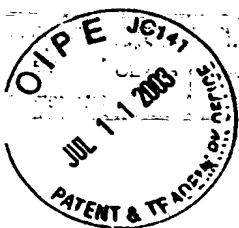


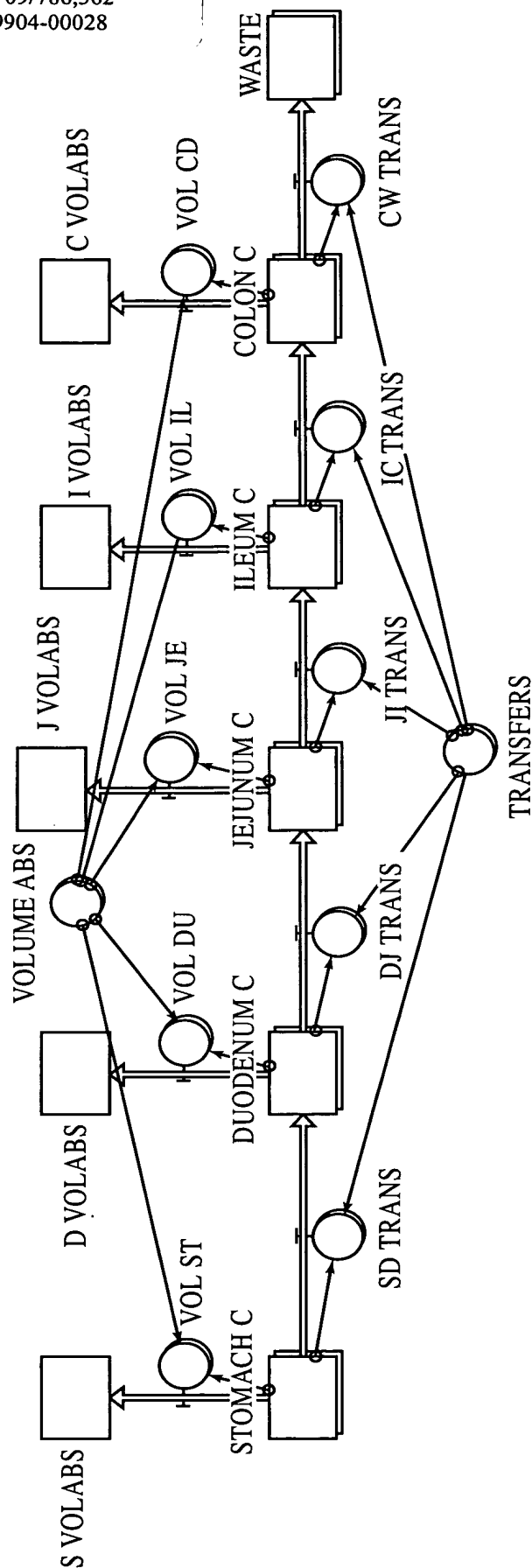
FIG.20





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FIG. 21
Gastrointestinal Transit



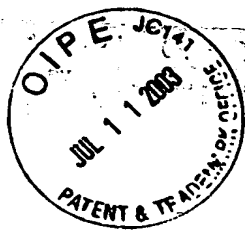
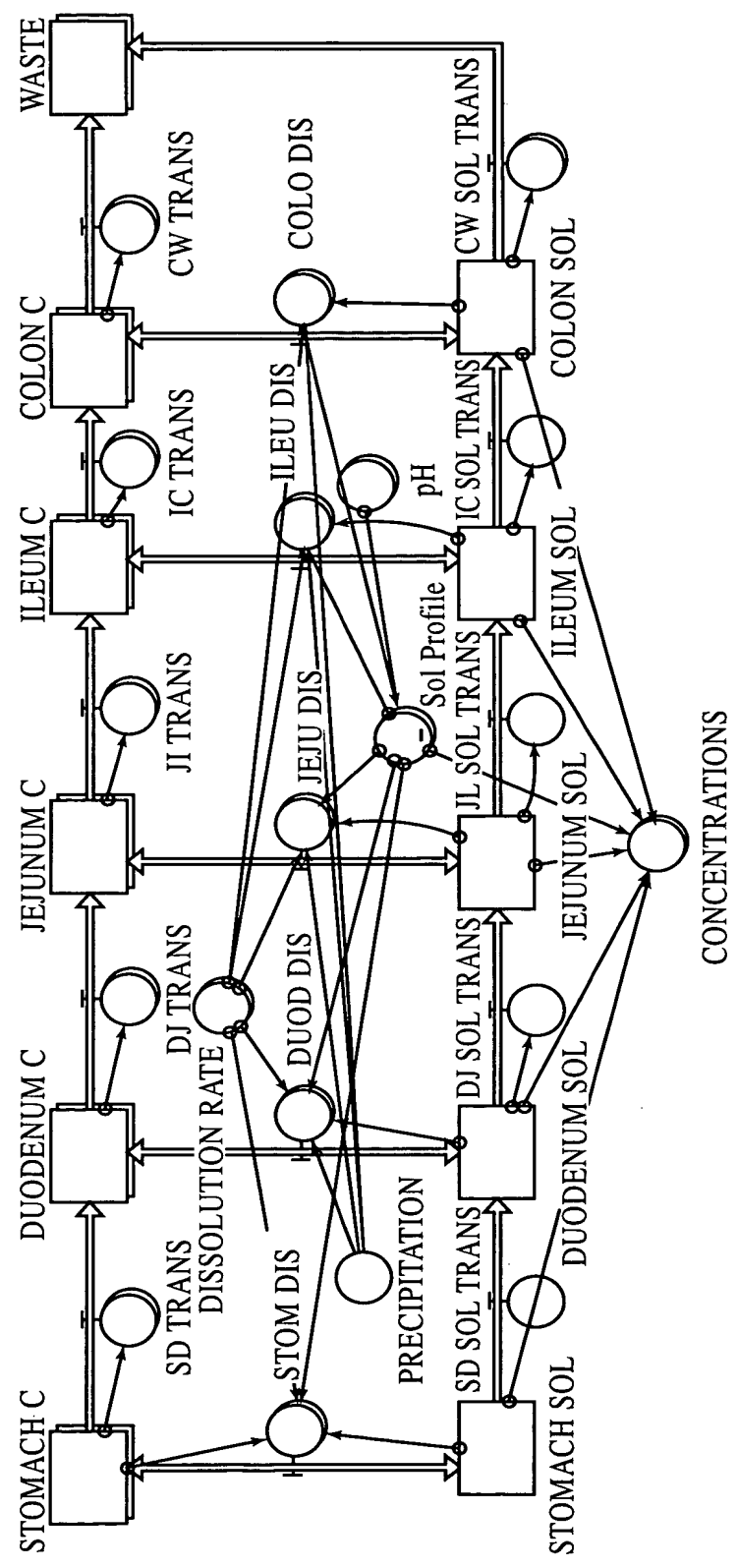
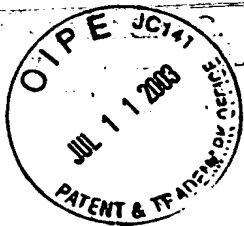


FIG.22
pH Dependent Solubility and Dissolution





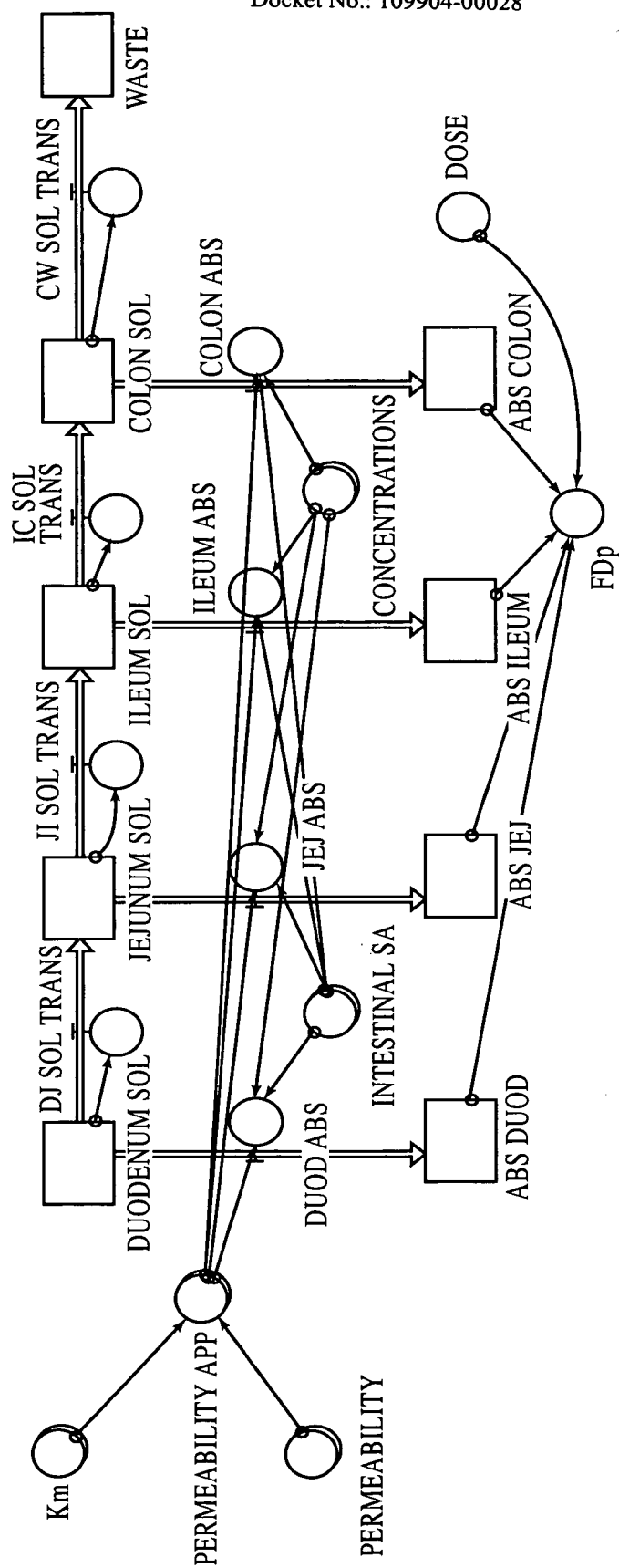
Title: METHOD FOR SCREENING AND PRODUCING COMPOUND LIBRARIES

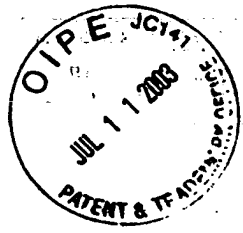
Inventor's Name: GRASS, et al.

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FIG.23
Absorption





Title: METHOD FOR SCREENING AND
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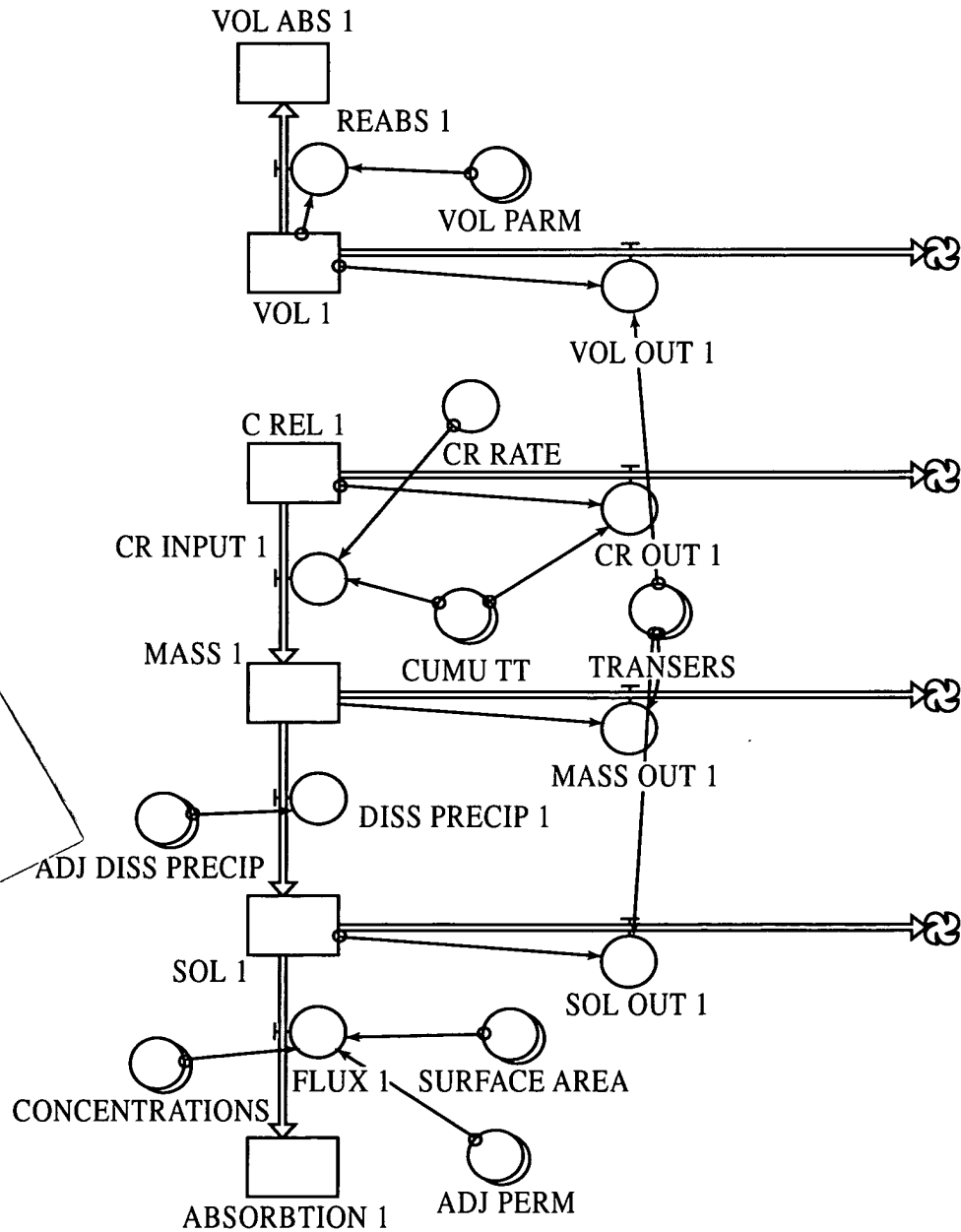
Inventor's Name: GRASS, et al.

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FIG.24

GI Tract-Intestinal Model



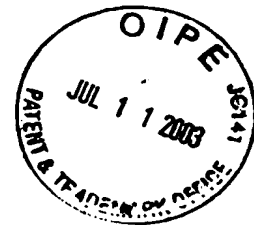
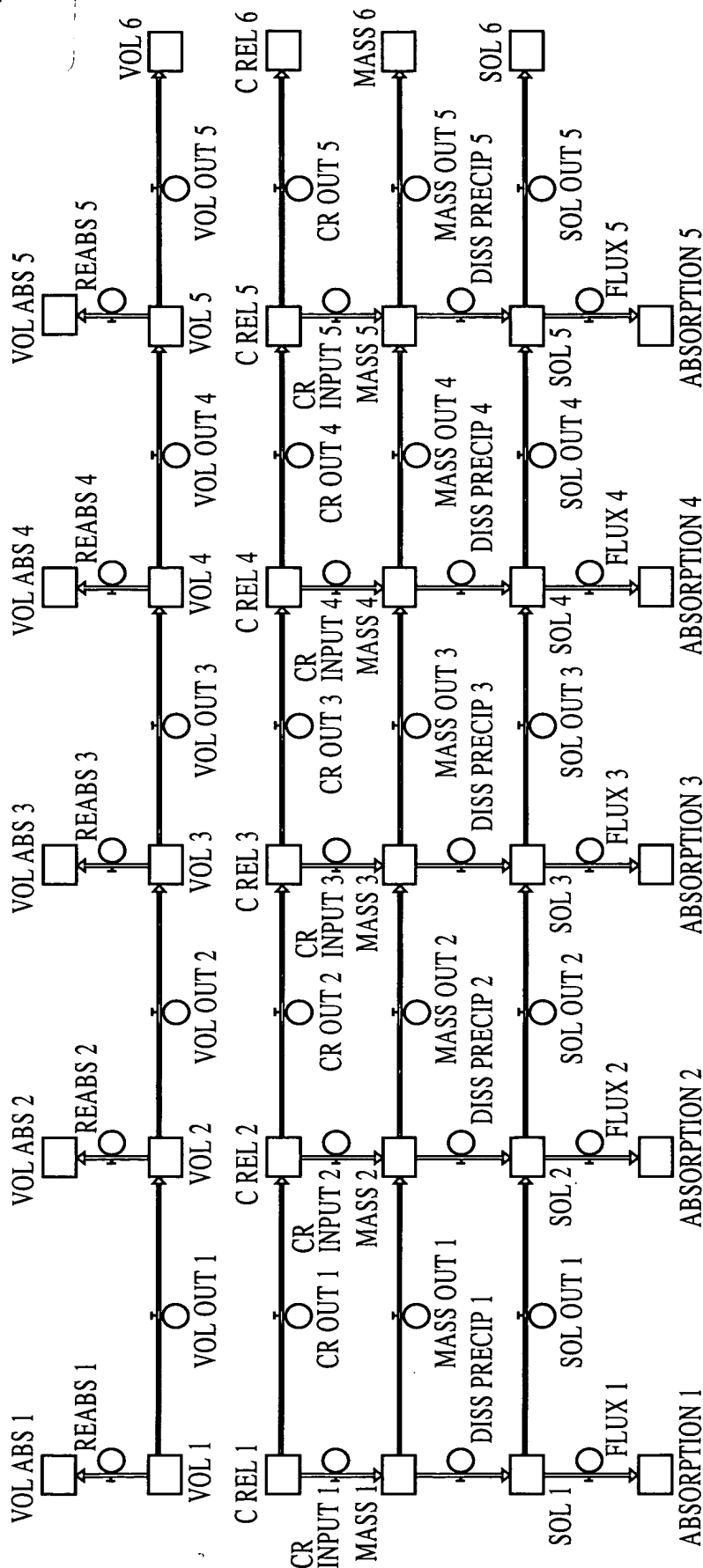
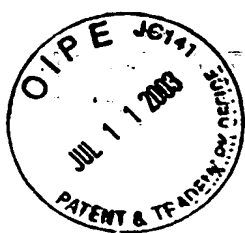


FIG.25
 GI Tract-Intestinal-Model (without converters, ghosts or connectors)



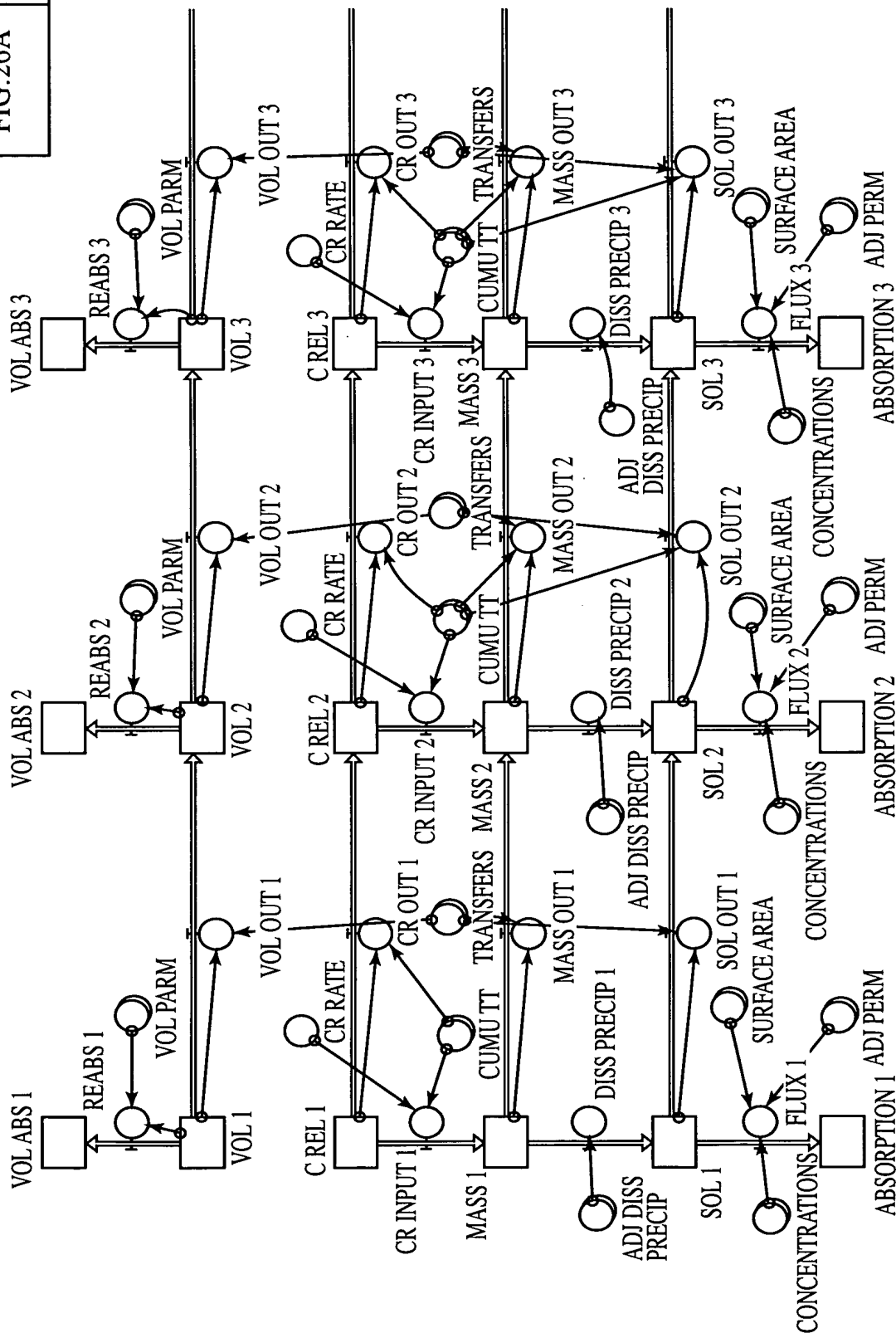


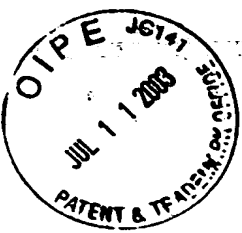
Title: METHOD FOR SCREENING AND
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FIG.26

FIG.26A

FIG.26B





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FIG.26B

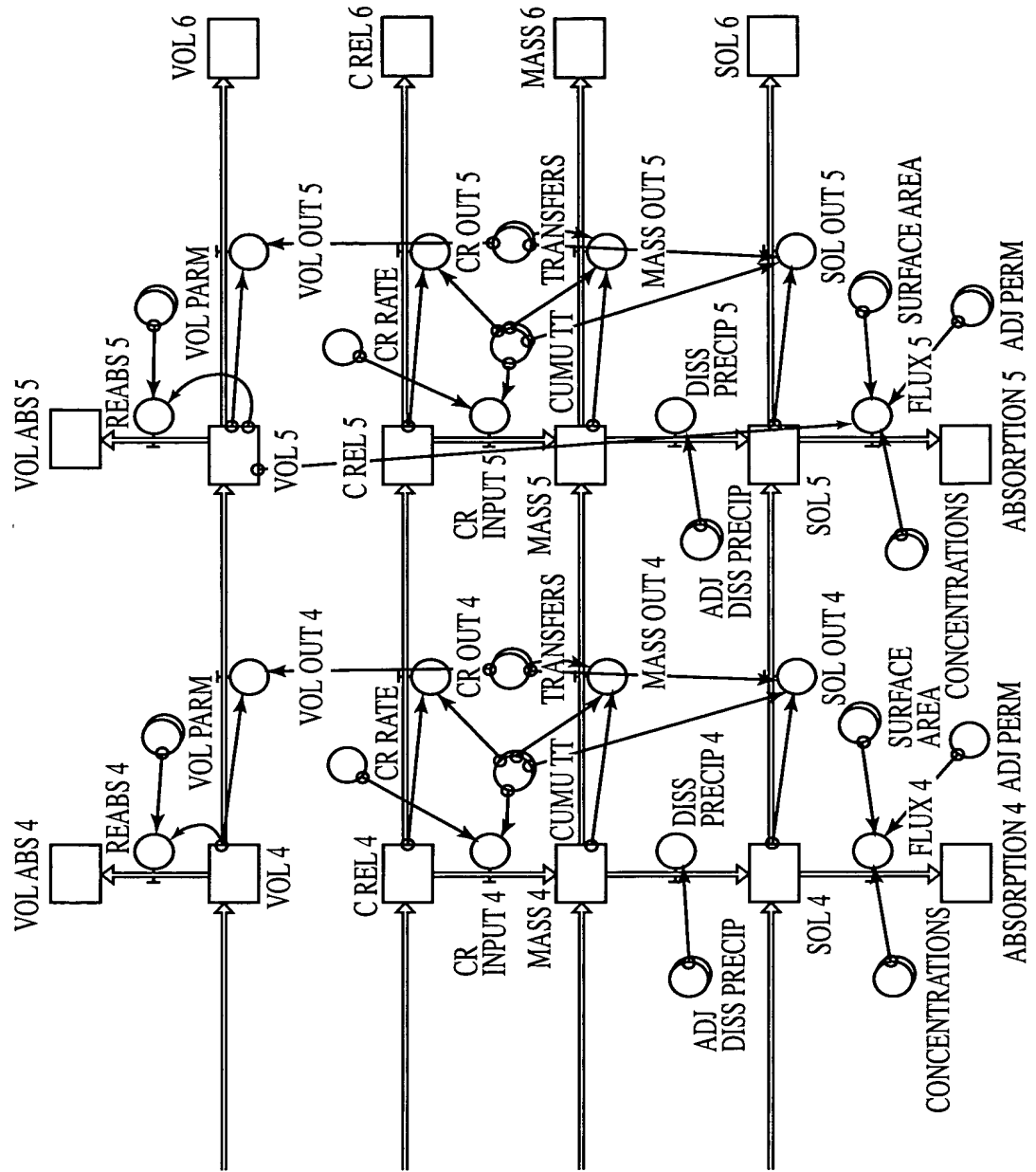
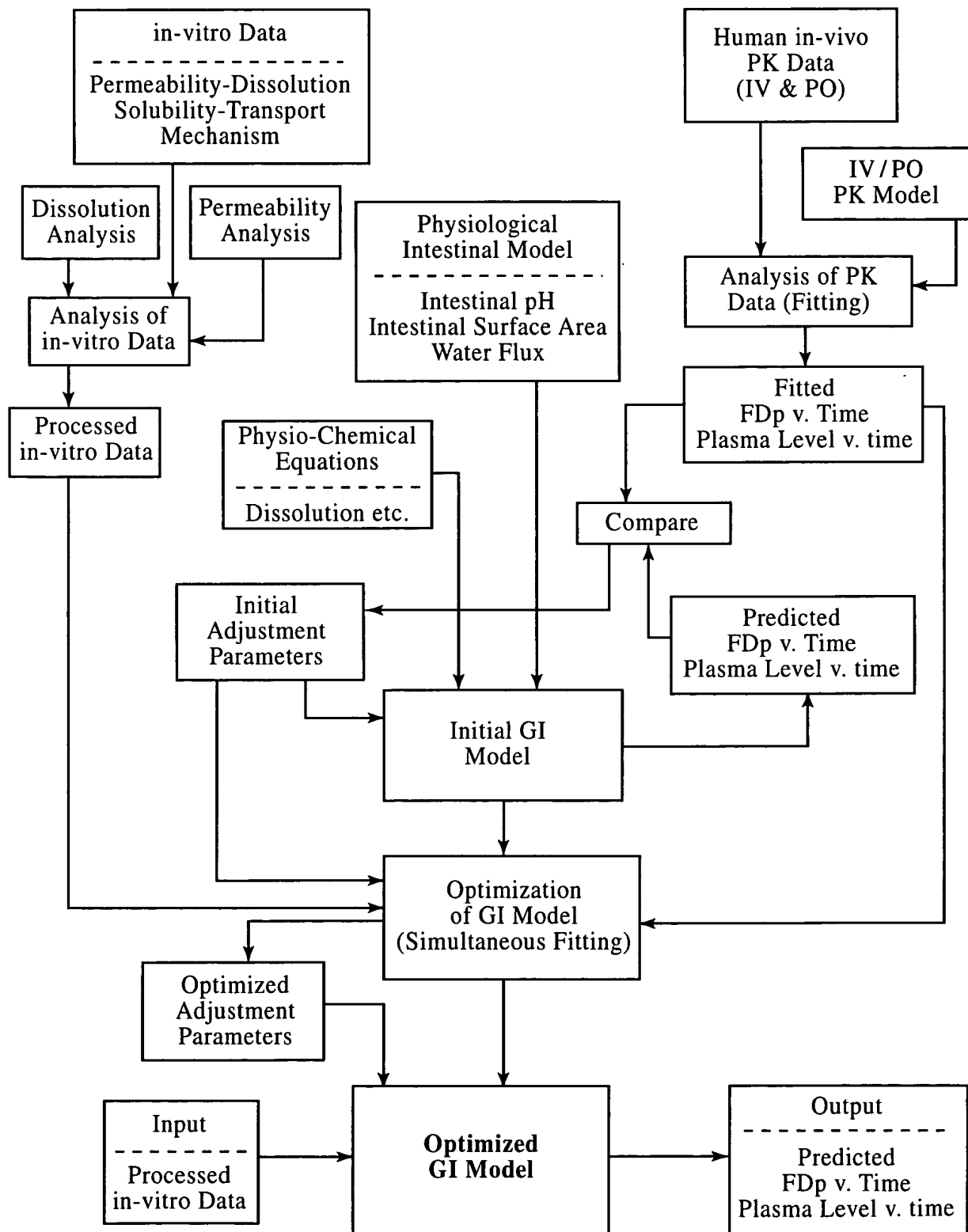




FIG.27



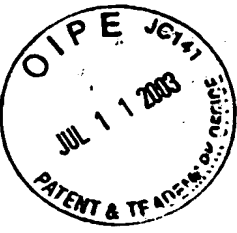


FIG.28

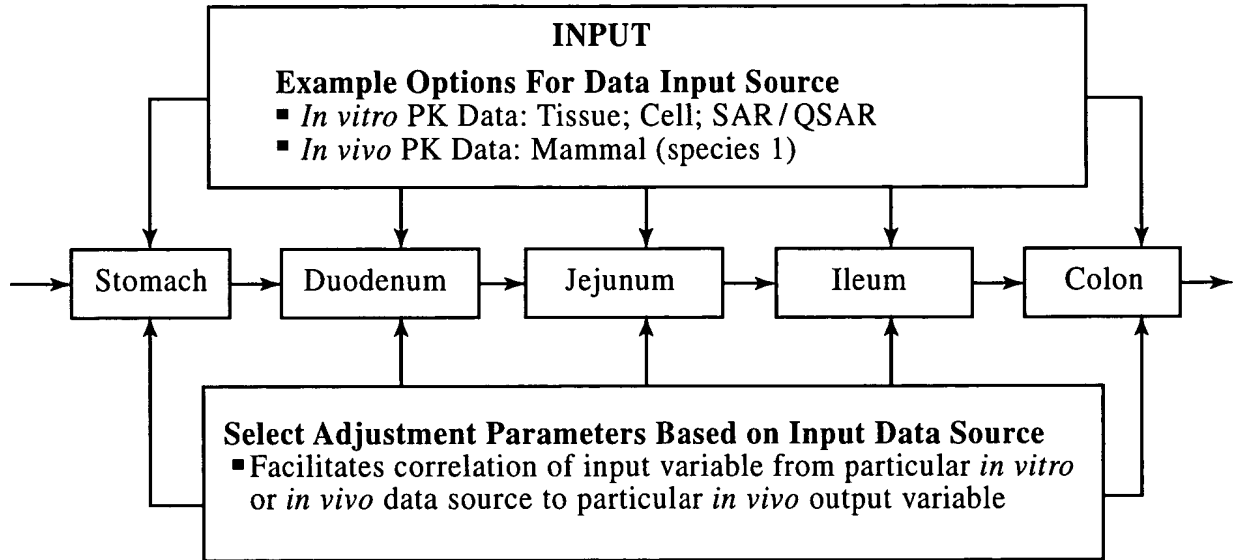
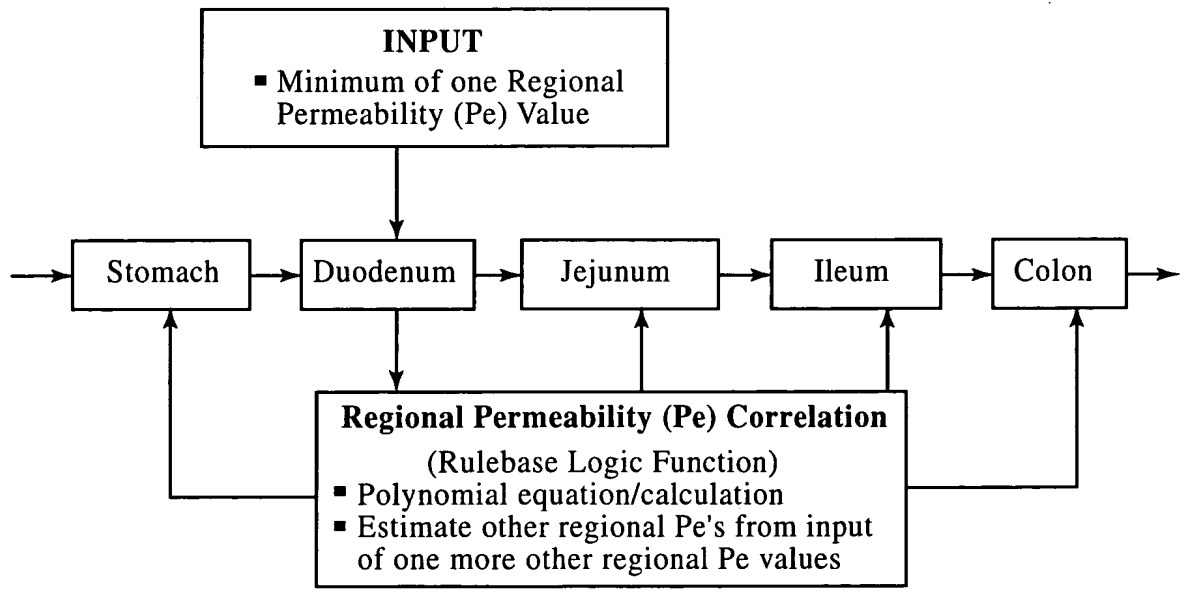


FIG.29





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FIG.30

Parameters

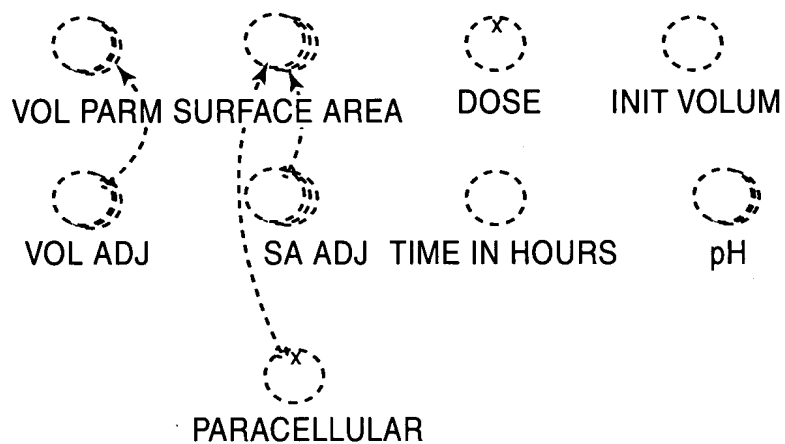
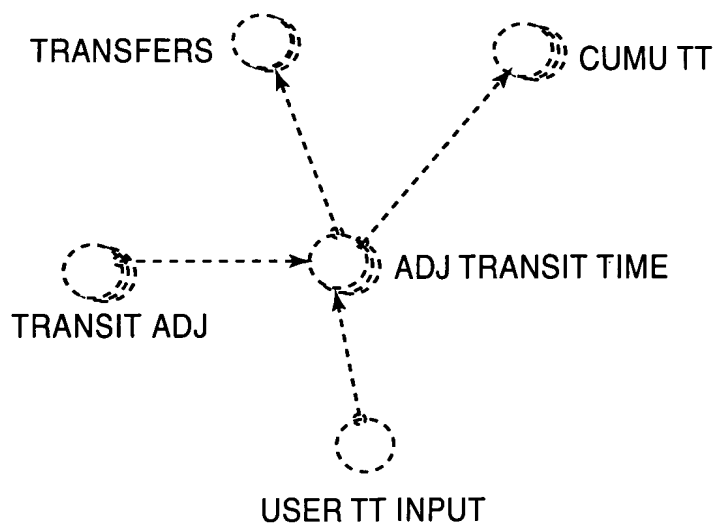


FIG.31

Transit Time



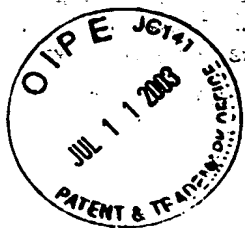


FIG.32

Permeability Calculation

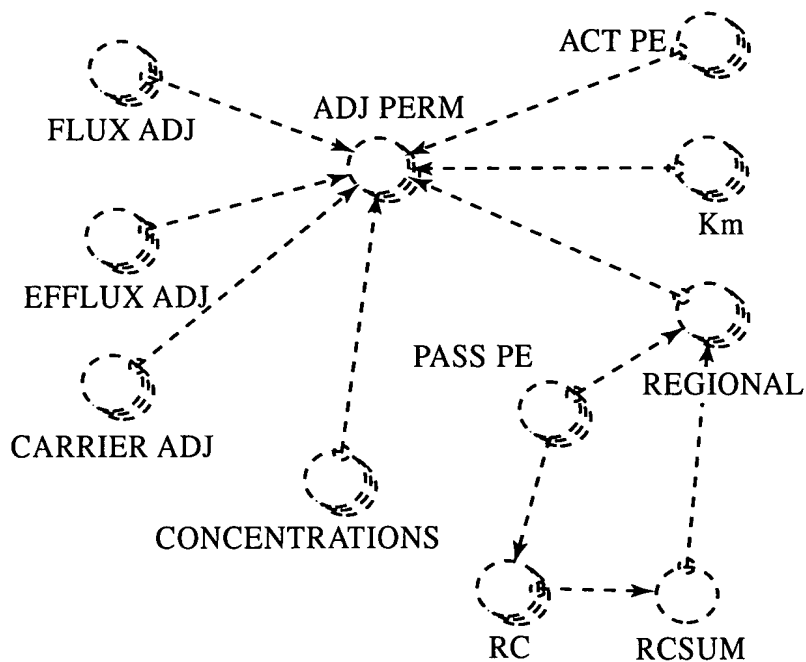
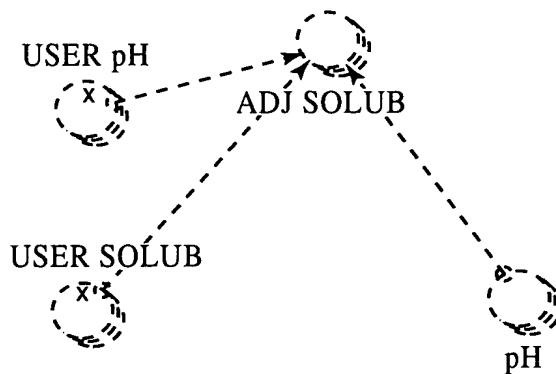


FIG.33

Solubility Calculation



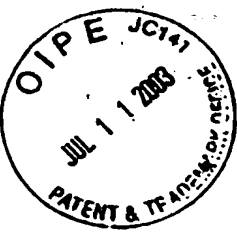


FIG.34

Control Release Calculation

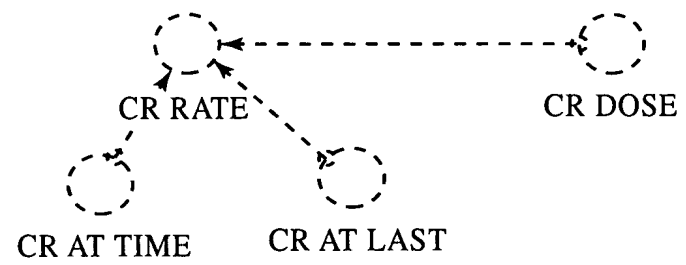
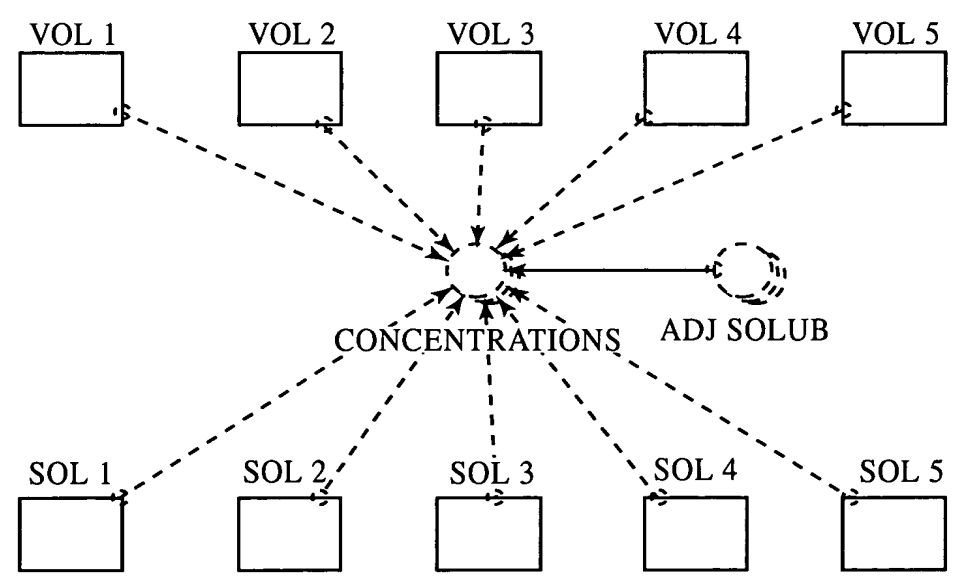
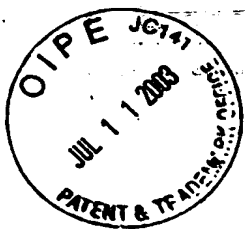


FIG.35

Concentration Calculation





Title: METHOD FOR SCREENING AND
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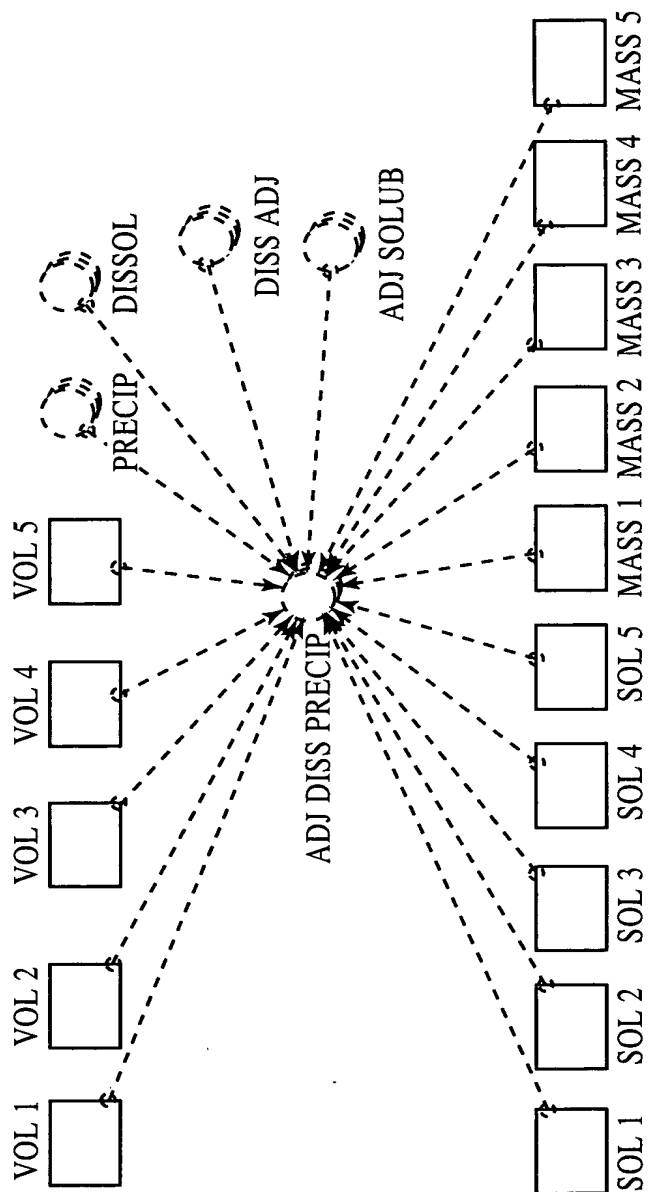
Inventor's Name: GRASS, et al.

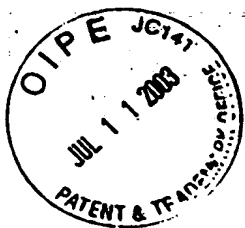
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FIG.36

Dissolution Calculation





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FIG.37

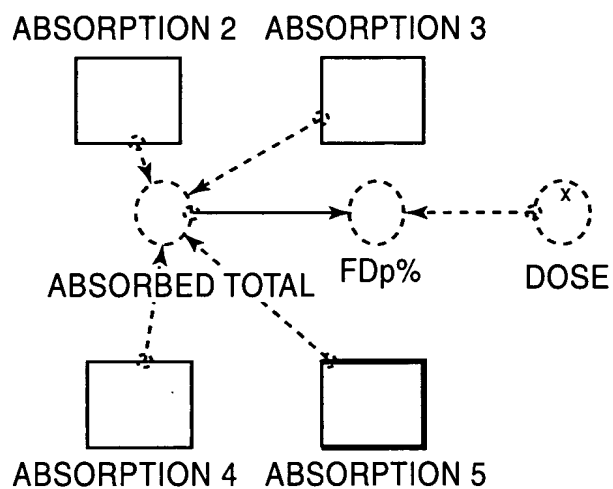
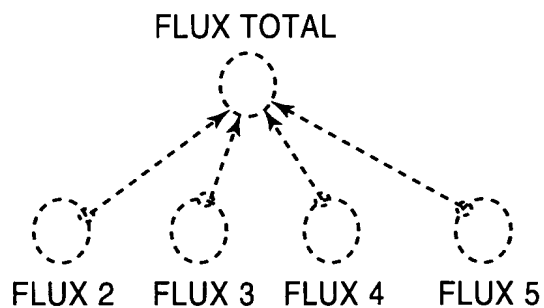
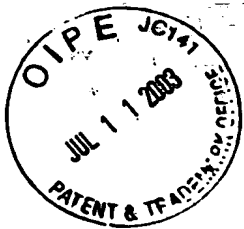


FIG.38





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FIG.39

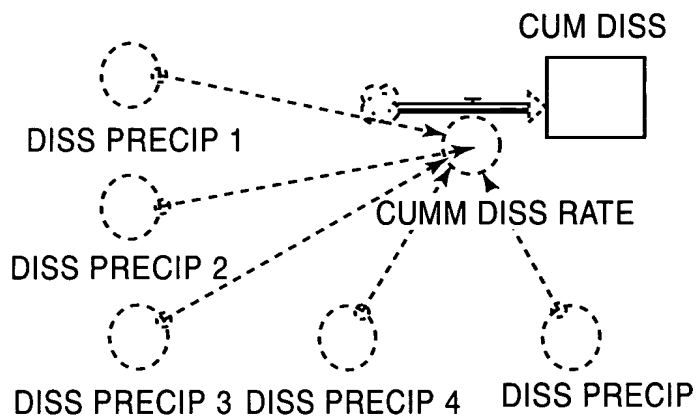
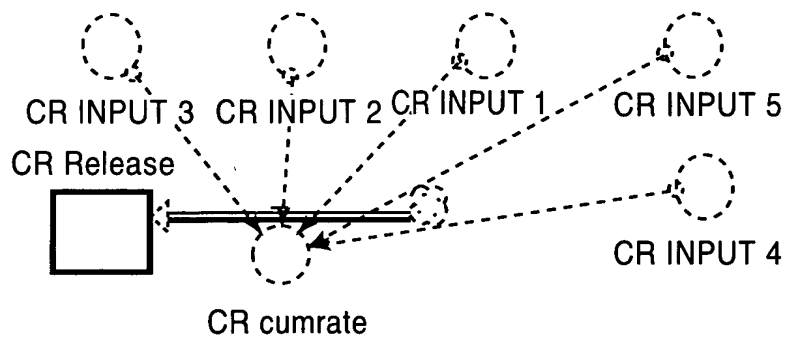


FIG.40



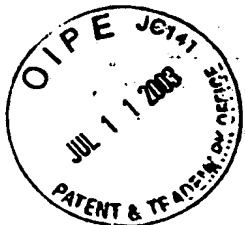


FIG.41

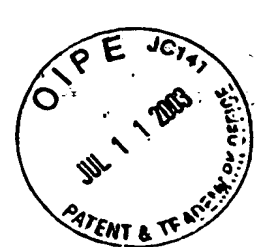
Physiological GI Tract Model

Database

- **GI Segment Compartments**
 - Fluid Absorption
 - Fluid Volume
 - Insoluble Mass
 - Soluble Mass
 - Soluble Mass Absorption
 - Dosage Form Mass
- **GI Segment Flow Regulators**
 - Fluid Absorption Rate
 - Fluid Volume Transit Rate
 - Insoluble Mass Transit Rate
 - Insoluble Mass Dissolution Rate
 - Soluble Mass Transit Rate
 - Soluble Mass Absorption Rate
 - Dosage Form Disintegration/Release Rate
- **GI Segment Converters**
 - Fluid Volume Absorption Rate Constant
 - GI Transit Rate Constant
 - Adjusted Dissolution Rate Constant
 - Dissolved Drug Concentration
 - Adjusted Surface Area
 - Adjusted Permeability

Rulebase

- GI Transit
- Dissolution
- Absorption
- Permeability Calculations
- Concentration Calculations
- Computational Error Corrections



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FIG.42

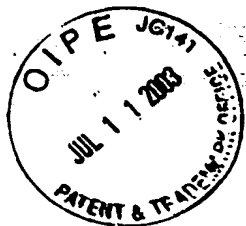
Physiological GI Tract Model

- **GI Segment Compartments & Flow Regulators**
 - **Fluid Absorption**
 - *Fluid Absorption Rate*
 - **Fluid Volume**
 - *Fluid Volume Absorption Rate*
 - *Fluid Volume Transit Rate*
 - **Insoluble Mass**
 - *Insoluble Mass Transit Rate*
 - *Insoluble Mass Dissolution Rate*
 - **Soluble Mass**
 - *Insoluble Mass Dissolution Rate*
 - *Soluble Mass Transit Rate*
 - *Soluble Mass Absorption Rate*
 - **Soluble Mass Absorption**
 - *Soluble Mass Absorption Rate*

FIG.43

Physiological GI Tract Model

- **GI Segments Flow Regulators & Converters**
 - **Fluid Absorption Rate**
 - *Fluid Volume*
 - *Fluid Volume Absorption Rate Constant*
 - **Fluid Volume Transit Rate**
 - *Fluid Volume*
 - *Fluid Volume Transit Rate Constant*
 - **Insoluble Mass Transit Rate**
 - *Insoluble Mass*
 - *Insoluble Mass Transit Rate Constant*
 - **Insoluble Mass Dissolution Rate**
 - *Insoluble Mass*
 - *Dissolution Rate Constant*
 - **Soluble Mass Transit Rate**
 - *Soluble Mass*
 - *Soluble Mass Transit Rate Constant*
 - **Soluble Mass Absorption Rate (Flux)**
 - *Surface Area*
 - *Dissolved Mass Concentration*
 - *Permeability*



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Inventor's Name: GRASS, et al.

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FIG.44

Physiological GI Tract Model

- **Converters**
 - Permeability
 - Passive Absorption Adjustment Parameter
 - Efflux/Secretion Adjustment Parameter
 - Active Absorption Adjustment Parameter
 - Active or Carrier Mediated Absorptive Permeability
 - Km
 - Passive Permeability/Regional Correlation
 - Passive Permeability
 - Logic Function For Regional Correlation
 - Passive Permeability
 - Logic Function For Regional Correlation
 - Dissolved Mass Concentrations
 - Dissolved Mass Concentration
 - Fluid Volume
 - Solubility
 - pH
 - Solubility
 - Dissolution Rate Constant
 - Fluid Volume
 - Precipitation Rate Constant
 - Dissolution Rate Adjustment Parameter
 - Solubility
 - Insoluble Mass
 - Soluble Mass
 - Surface Area
 - Surface Area Adjustment Parameter
 - Transport Mechanism
 - Transit Rate
 - Transit Time Adjustment Parameter
 - User Adjusted Transit Time
 - Fluid Volume Absorption Rate Constant
 - Fluid Volume Adjustment Parameter

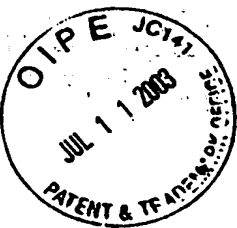


FIG.45

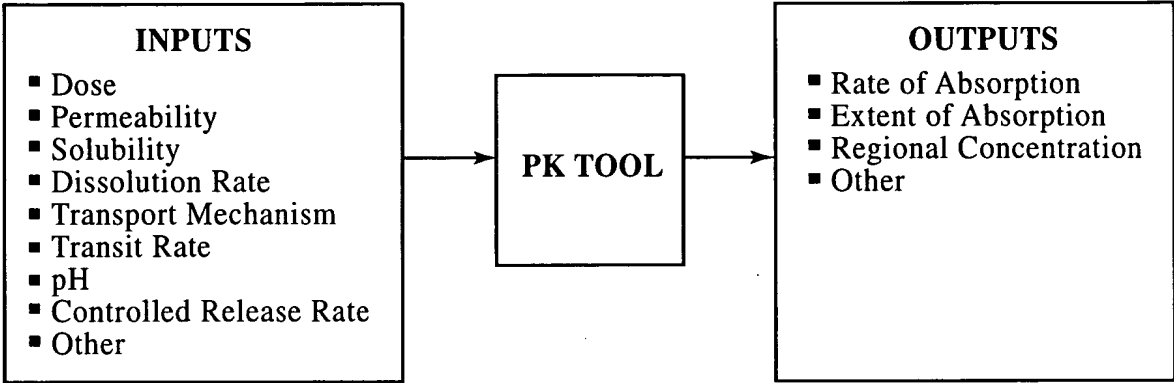
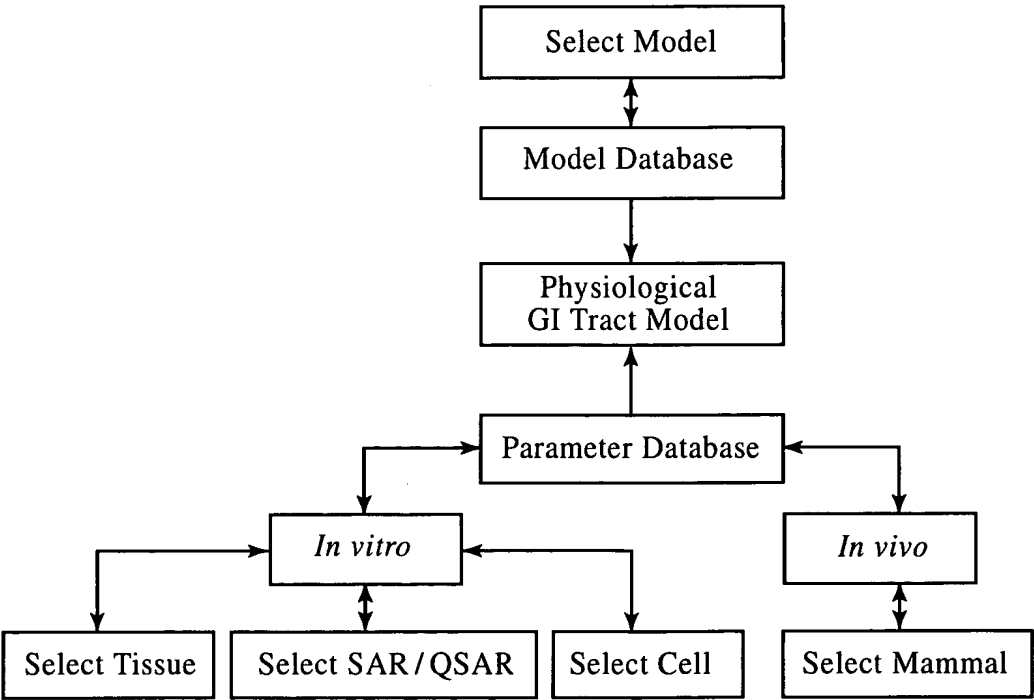
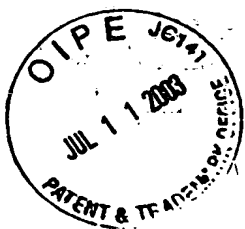


FIG.46





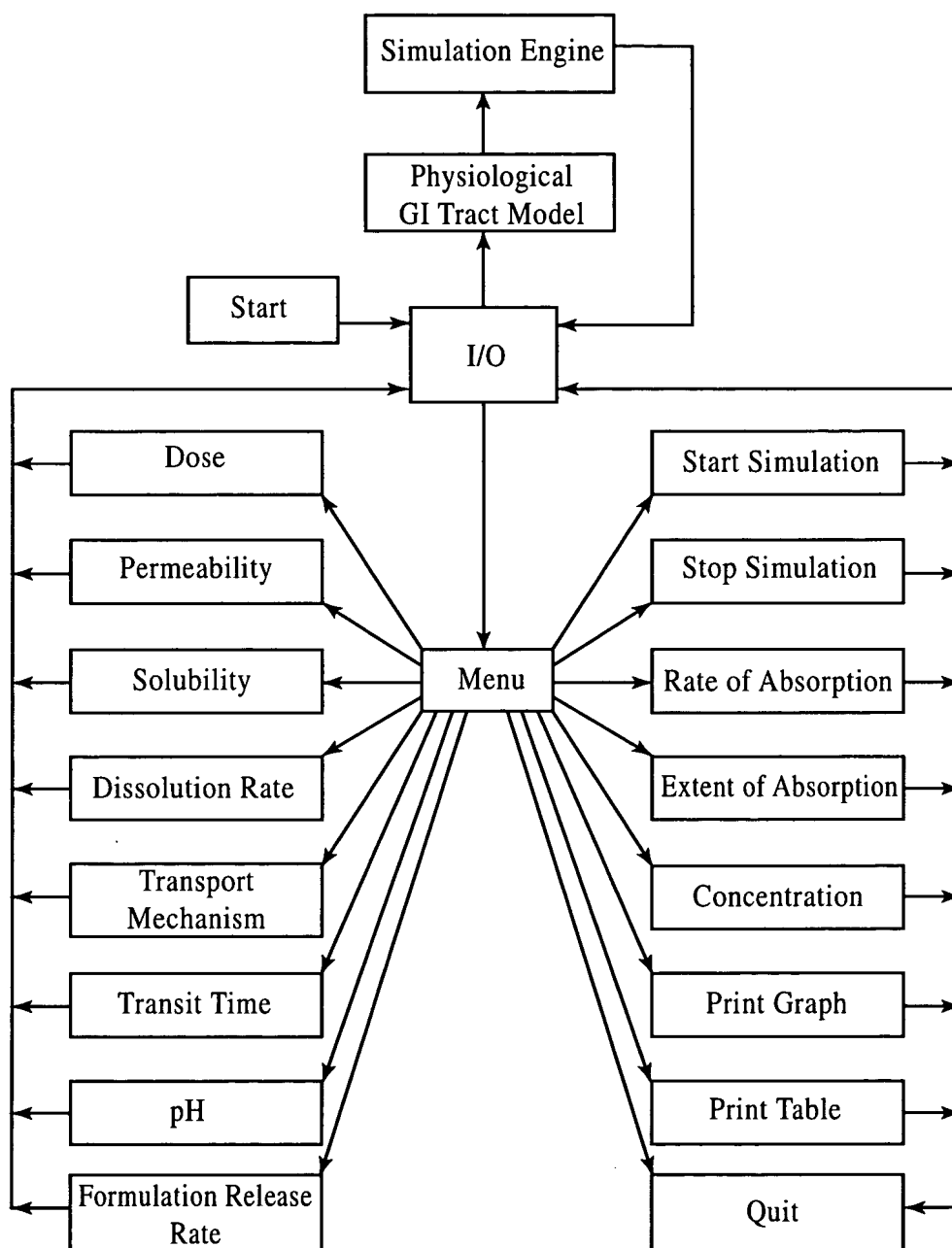
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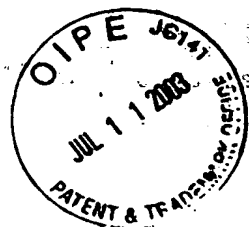
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FIG.47





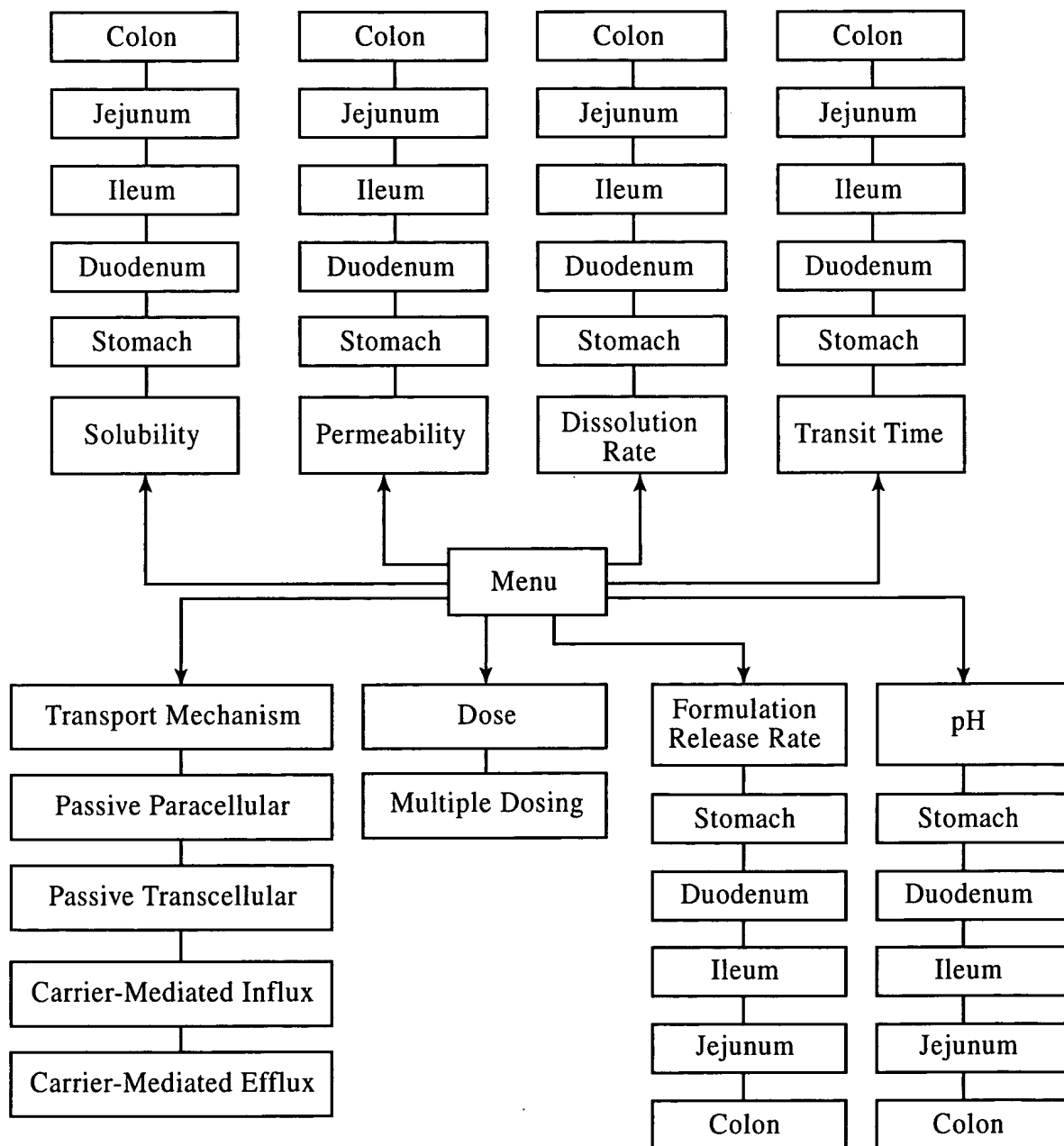
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FIG.48





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FIG.49

Correlation of FDp Extent-GI Model and Pharmacokinetic data

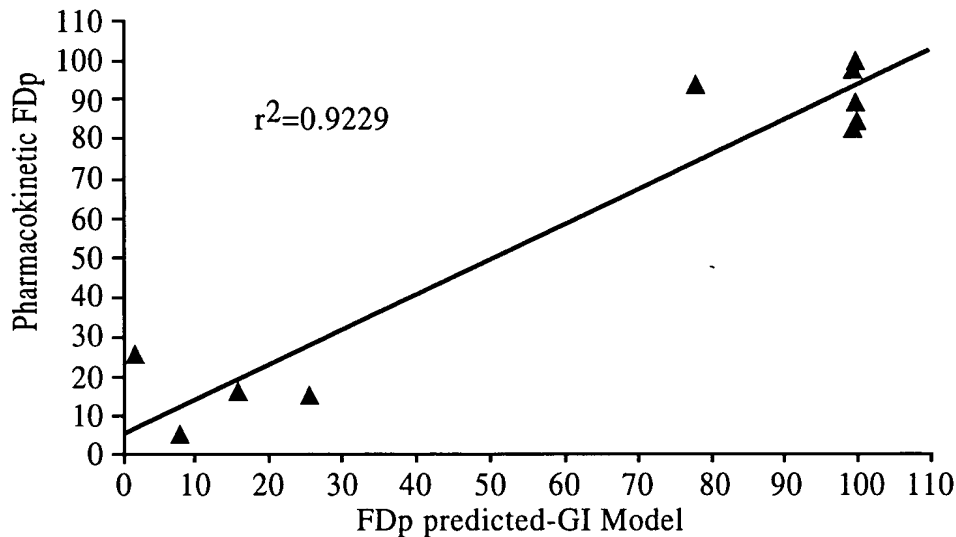
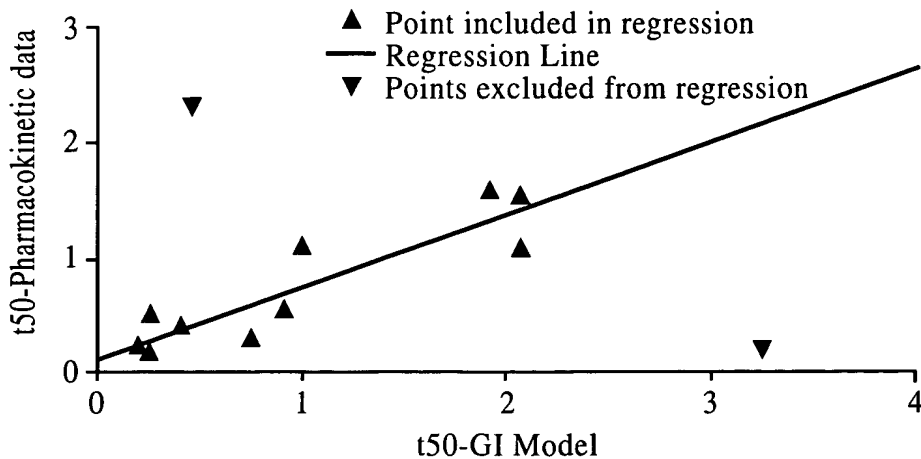
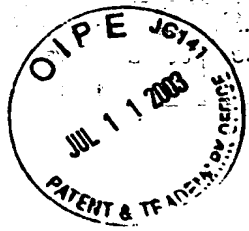


FIG.50

Correlation of FDp rate of absorption-GI Model and
Pharmacokinetic Data





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FIG.51

PO Pharmacokinetic Data
Compound $\alpha 1$

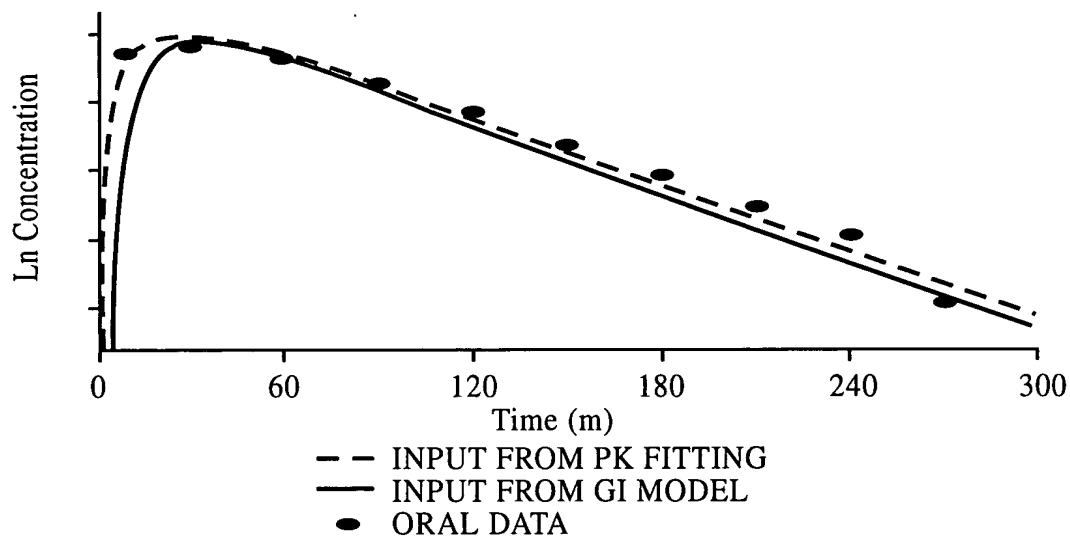
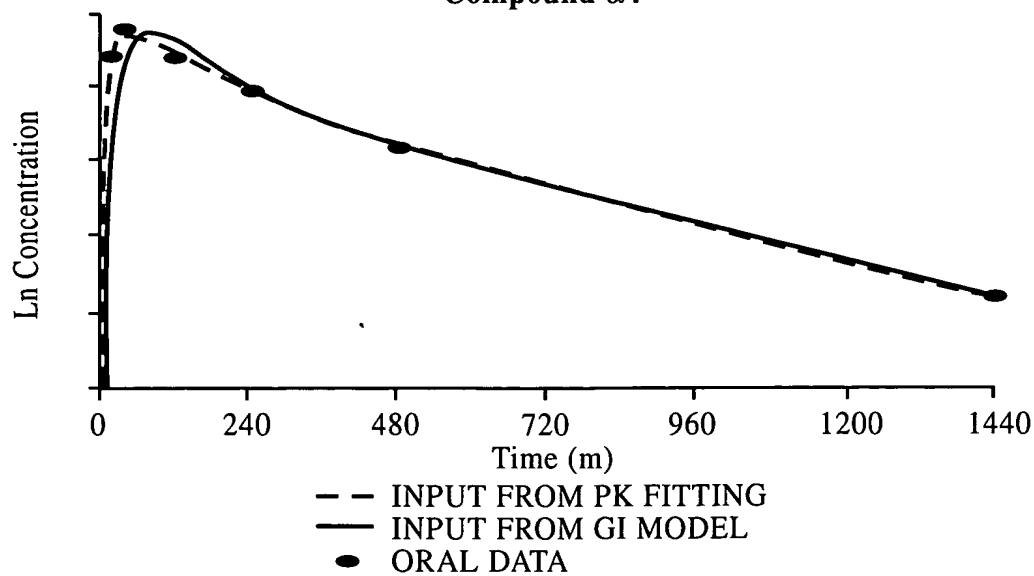
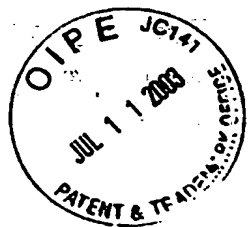


FIG.52

PO Pharmacokinetic Data
Compound $\alpha 4$





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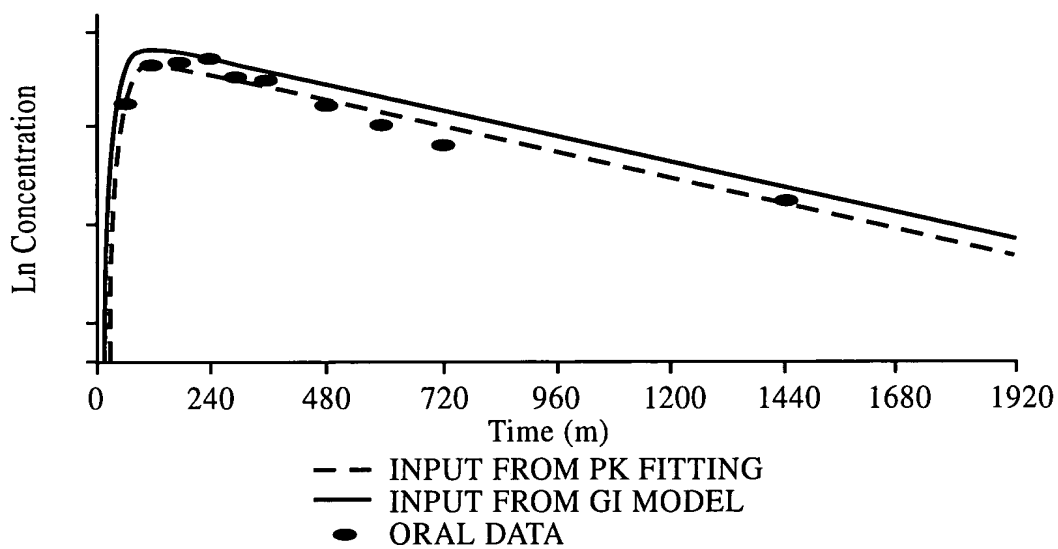
Inventor's Name: GRASS, et al.

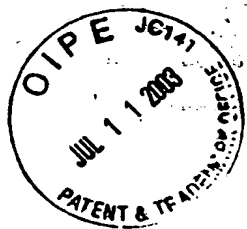
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Docket No.: 109904-00028

FIG.53

PO Pharmacokinetic Data
Compound β_6





SUBCLASS

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FIG.54

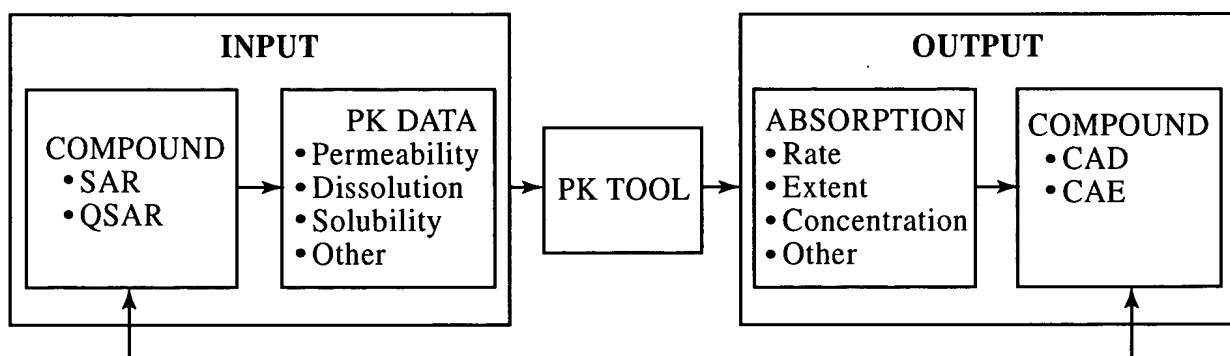


FIG.55

